

# AMERICAN JOURNAL OF OPHTHALMOLOGY

THIRD SERIES FOUNDED BY EDWARD JACKSON

## CONTENTS

Alterations of vitreous body .....	<i>Charles L. Schepens</i>	631
Tapetoretinal degeneration .....	<i>J. François and G. Decock</i>	633
Hereditary macular degeneration .....	<i>C. Truman Davis and Robert W. Hollenhorst</i>	637
Congenital retinal fold .....	<i>Stefan Van Wien and W. B. Sullivan</i>	643
Macular holes in retinal separations .....	<i>Arthur H. Keeney</i>	648
Treatment of tuberculous choroiditis .....	<i>James E. Lebensohn</i>	653
Calcified scleral nodules .....	<i>Samuel Gartner and Karl Rubner</i>	658
Tuberous sclerosis .....	<i>William Joachim Pagenstecher</i>	663
Vitreous hemorrhage absorption .....	<i>R. A. Schimek and E. H. Steffensen</i>	677
Mechanism of miopiesin formation .....	<i>Ernst Schmerl, Albert A. Dietz and Bernhard Steinberg</i>	684
Antibiotics and herpes simplex .....	<i>Ruth G. MacKneson and H. L. Ormsby</i>	689
Ocular use of tetracycline .....	<i>J. W. Hallett, Khalida Naib and Irving H. Leopold</i>	691
Curare administration .....	<i>Oscar Dablène and J. Wesley McKinney</i>	697
Influence of coffee on ocular tension .....	<i>W. Leydhecker</i>	700
Flicker-fusion and hypertension .....	<i>Jordan M. Scher and Willard H. Spankus</i>	705
Cataract operation in office .....	<i>Lyndon Evelyn</i>	715
Objective refraction methods .....	<i>David Volk</i>	719
Syringomyelia .....	<i>Norman Yourish, Nathaniel Wollin and Arthur Nathaniel</i>	728
Streptokinase and streptodornase .....	<i>Arthur Sacks-Wilner, S. Sinclair and Truman Boyes</i>	730
Congenital neuroparalytic keratitis .....	<i>Walter Segall</i>	732
Hemianopsia and papilledema .....	<i>B. G. Prater and Robert L. Lam</i>	738

## DEPARTMENTS

Society Proceedings .....	742	Obituaries .....	762	Abstracts .....	770
Editorials .....	758	Correspondence .....	763	News Items .....	789
		Book Reviews .....	766		

For complete table of contents see advertising page xix

Publication office: 450 Ahnaip St., Menasha, Wisconsin

Copyright, 1955, Ophthalmic Publishing Company, 664 North Michigan Avenue, Chicago 11, Illinois

Subscription price in United States twelve dollars yearly. In Canada and foreign countries fourteen dollars. Published monthly by the Ophthalmic Publishing Company. Subscription and Advertising Office: 664 North Michigan Avenue, Chicago 11, Illinois. Entered as second class matter at the post office at Menasha, Wisconsin. Printed in U.S.A.



# Complete ARTIFICIAL EYE Service

Experience gained through over 100 years of artificial eyemaking enables us to produce and fit the very finest in artificial eyes. Glass and plastic eyes made to order or available from stock. Eyes fitted to all types of motility implants.

**fitting of  
artificial eyes  
through the mail**

Orders filled the same day received  
Eyes sent on memorandum  
Liberal assortment of either glass or plastic  
Samples accurately matched  
Superior quality eyes—Finest workmanship

*Serving the  
Profession  
Since 1851*

**Mager and Gougelman, inc.**

30 NORTH MICHIGAN AVENUE • CHICAGO 2, ILLINOIS

DETROIT • CLEVELAND • KANSAS CITY • MINNEAPOLIS • NEW ORLEANS • ST. LOUIS  
NEW YORK • BOSTON • BUFFALO • PHILADELPHIA • PITTSBURGH • WASHINGTON

PAUL GOUGELMAN COMPANY

30 NORTH MICHIGAN AVENUE • CHICAGO, ILLINOIS



**Upjohn**

# Cortef\* for inflammation, neomycin for infection:

---

*Each cc. contains:*

Hydrocortisone acetate 15 mg. (1.5%)

Neomycin sulfate 5 mg.  
(equiv. to 3.5 mg. neomycin base)

Preserved with myristyl-gamma-  
picolinium chloride 1:5000

*Supplied:*

Bottles of 2.5 cc. and 5 cc. with dropper.

*Application:*

Useful both in the eye and the  
external ear canal.

\*REGISTERED TRADEMARK FOR THE UPJOHN BRAND OF  
HYDROCORTISONE (COMPOUND F)

\*\*REGISTERED TRADEMARK FOR THE UPJOHN BRAND OF  
HYDROCORTISONE WITH NEOMYCIN SULFATE

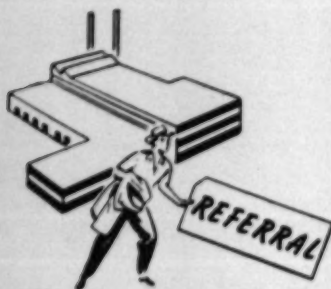
The Upjohn Company, Kalamazoo, Michigan

# Neo-Cortef<sup>®</sup> drops

STERILE SUSPENSION



**5,000,000 workers  
needed professional  
eye care**



Visual skills of more than 12,000,000 workers have been tested through the Bausch & Lomb Occupational Vision Service. Of these, about 42%—more than 5,000,000—have been found to be in need of professional eye care.

Now the same tests of visual performance can be made in your office. Use the Bausch & Lomb Professional Ortho-Rater for pre-refractive and post-refractive evaluation of the twelve visual skills. And for referred Occupational Vision patients it provides objective evidence of improvement resulting from professional care.

**BAUSCH & LOMB**

**Professional  
Ortho-Rater**

**... A NEW PRECISION  
TESTING INSTRUMENT  
FOR PROFESSIONAL  
MEASUREMENT OF  
VISUAL SKILLS**



**BAUSCH & LOMB**



# Terra-Cortril

brand of oxytetracycline and hydrocortisone

**ophthalmic suspension**

**when the  
ophthalmologic  
picture**

**is due to  
double exposure**

**Terra-Cortril** Ophthalmic Suspension rapidly clears both underlying inflammation and superimposed infection through the combined actions of CORTIL®—most potent anti-inflammatory adrenocortical steroid;<sup>1</sup> and TERRAMYCIN®—broad-spectrum antibiotic “highly successful against many varieties of organisms” encountered in ophthalmologic practice.<sup>2</sup>

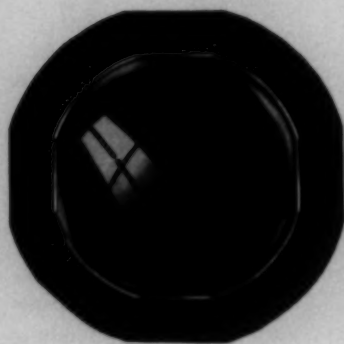
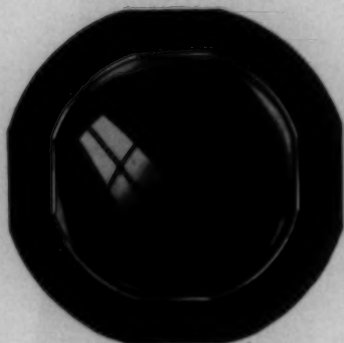
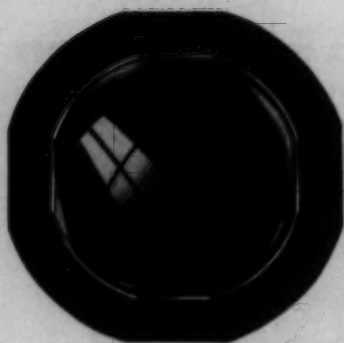
**supplied:** in amber bottles of 5 cc., with sterile eye dropper, containing 5 mg. TERRAMYCIN (oxytetracycline hydrochloride) and 15 mg. CORTIL (hydrocortisone acetate) per cc. of sterile suspension. **also available:** CORTIL Acetate Ophthalmic Ointment and CORTIL Tablets.

1. Rukes, J. M., et al.: *Metabolism* 3:481, 1954. 2. Cannon, E. J., and Leopold, I. H.: *A.M.A. Arch. Ophth.* 47:426, 1952.

PFIZER LABORATORIES



Division, Chas. Pfizer & Co., Inc. Brooklyn 6, New York



### Precision Vision from Every Angle

Shuron Widesite Corrected Curve Lenses...either White or Tonetex... give your patients clear, undistorted vision from edge to edge of the lenses, by correcting for marginal astigmatism within acceptable limits.

### Always and Only First Quality

Widesite Corrected Curve Lenses are always and only First Quality. They're free from surface aberration...polished to mirror finish. No seeds, striae, bubbles or other internal flaws. Correctly centered, with precision curves and exact powers. Accurately controlled thickness.

### Corrected Curve Lenses

Specify Widesite for faithful interpretation of your Rx. A complete range of Corrected Curves—in White and Tonetex—from your independent Laboratory.



Shuron Optical Company, Inc.  
Geneva, N.Y.

W

I

D

E

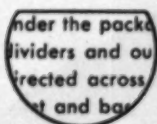
S

I

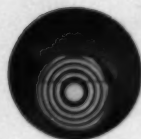
T

E

**SHURON**



**design and performance**



**manufacturing quality**



**patient acceptance**



**service**



put them all together, they spell



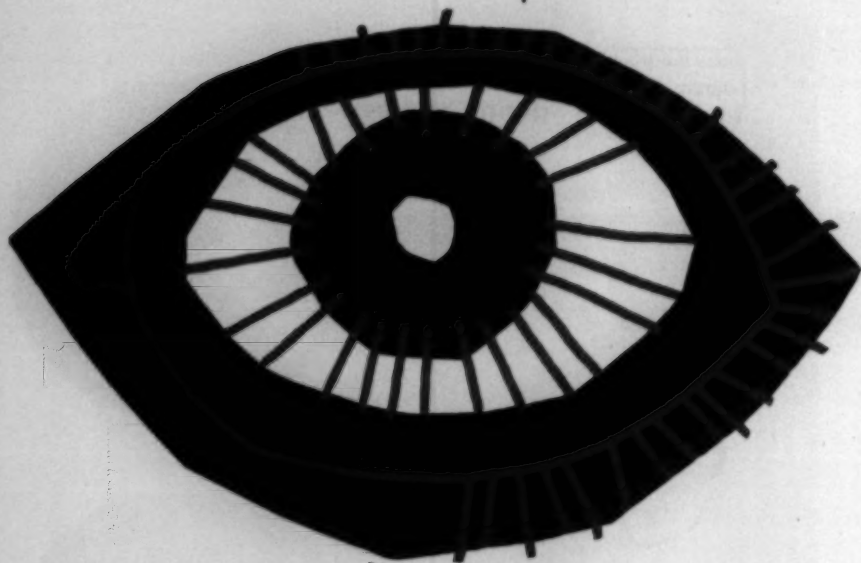
Superior design? Superior performance? Ask the imitators! But the Univis quality standards which contribute so much to patients' satisfaction with your Rx can't be imitated. Quickly available from the nation's top laboratories.

THE **Univis** LENS COMPANY • Dayton, Ohio • New York, Chicago, Los Angeles, San Francisco



COMMAND PERFORMANCE FRAMES • MASCULON • ENSEMBLE





for coccic infections  
... and in trachoma

**Erythrocin<sup>®</sup>** LACTOBIONATE, 1%,  
OPHTHALMIC OINTMENT

Backed by extensive clinical trials—ERYTHROCIN Lactobionate Ointment is highly effective against staph-, strep- and pneumococcic eye infections . . . as well as in acute and chronic stages of trachoma. You'll find that ERYTHROCIN quickly penetrates the ocular tissues and appears in the aqueous humor. In addition, you'll find ERYTHROCIN Lactobionate Ointment especially useful *when the infecting organism resists other antibiotic ointments*. It comes in boxes of 12 1/8-ounce tubes. Each tube has a tip for ointment instillation into the conjunctival sac. Try ERYTHROCIN Lactobionate Ointment.

**Abbott**



**new corneal anesthetic**  
**rapid action and**  
**short duration\***

**virtually nonsensitizing**

no cases reported of dermatitis occurring in patient's eye or on hands of physician.

**relatively nonirritating**

does not sting or burn when dropped into the eye—changes in the corneal epithelium or hyperemia of the conjunctiva rarely occur.

*Average dose: for tonometry, 2 drops. For minor surgical procedures, 2 drops instilled 3 times at 90 second intervals.*

Supplied: sterile normal saline solution with 0.02% Butoben as preservative, and containing 0.4% Dorsacaine Hydrochloride (benoxinate hydrochloride). In ½ oz. plastic squeeze bottle with dropper tip which delivers uniform drops (approximately 45 drops per cc.).

\*Schlagel, H. E., Jr., and Swan, E. C.: A.M.A. Arch. Ophth. 51: 583 (May) 1954.

council accepted



# DORSACAINE®

HYDROCHLORIDE

SMITH-DORSEY • Lincoln, Nebraska • A Division of The Wander Company

**Storz**  
*Surgical Instruments*

**NEW • LIGHT • POWERFUL**



## STORZ ATLAS **Hand Eye Magnet**

**I-6650**—Eye Magnet, Atlas: complete with four tips in wooden case and separate rectifier with footswitch. Small size for maneuverability and ease of handling. The magnet weighs 4.6 lbs. The rectifier with footswitch weighs 8.7 lbs. The type of tip selected is dependent on the position of the splinter. For strongest pulling power, the large cone tip is applied. More effective results are obtained by stepping on the footswitch repeatedly to get short interrupted pull rather than a long steady pull.

### **Power:**

The strong pulling power is similar to that given by the giant magnet. The absolute pulling power at the flange is 12.5 kg. or 28 lbs. The ball jump power is 38.3 mm. The handling is not interfered with by strong directional pulls.

### **Advantages...**

**Small size**—maneuverability

**Light weight**—easily handled

**Versatile**—selection of tips

**POWER! — POWER! — POWER!**

Storz Instruments are available from Storz salesmen only. We do not distribute under any other name or trademark.

Made for 110 volt, 60 cycle, alternating current. If other current or voltage is desired, please specify. Uses 150 watts.

Developed and tested at the University Eye Clinic in Kiel.

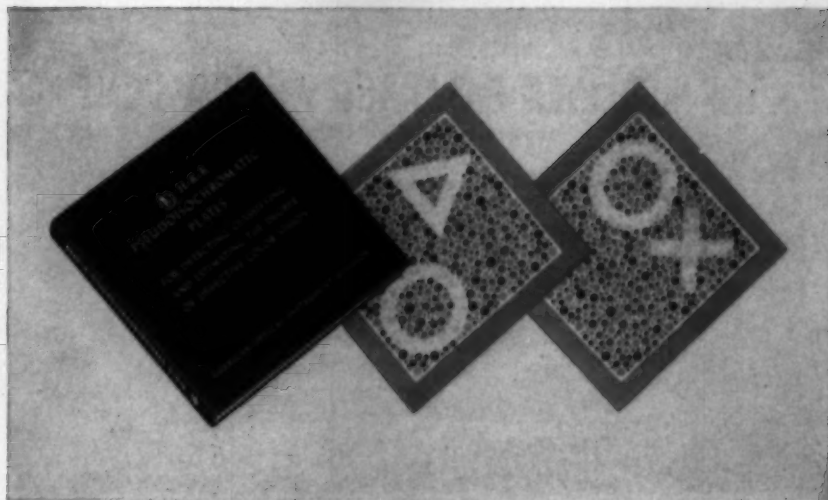
**Complete—\$149.50**

Order directly from

**Storz Instrument Company**

4570 Audubon Ave.

St. Louis 10, Mo.



# *Announcing* **The NEW AO<sup>®</sup> H-R-R PSEUDOISOCROMATIC PLATES**

LeGrand H. Hardy, M.D.  
by Gertrude Rand, Ph.D.  
M. Catherine Rittler, B.A.

Based on the research work originally conducted in the Knapp Memorial Laboratory of Physiological Optics, the Institute of Ophthalmology of Presbyterian Hospital and the Department of Ophthalmology of the College of Physicians and Surgeons of Columbia University, New York, New York.

American Optical announces the most comprehensive low-cost color test ever produced. Many years in development, it has a scope, and thoroughness never before achieved in a test of this type. Extremely easy to administer, it makes complete, accurate color vision testing a logical facility of every office.

First, it separates people with defective Red-Green and/or Blue-Yellow color vision from those with normal color vision. Further, it classifies the subject's defect as to Protan, Deutan, Tritan or Tetartan. Finally it estimates the amount of the deficiency as mild, medium or strong.

The development of the test has been so successful that it combines speed and ease of administration with the new fea-

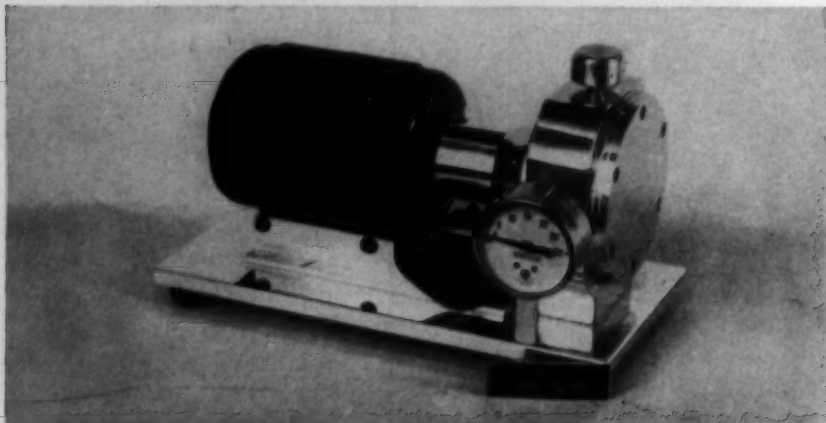
tures of classification and quantitative diagnosis. For the vast majority of people the test is completed in seconds. The symbols used are universally understood. The ingenious pattern of the plates allows no clues for memorization. It has been approved by the Subcommittee on Color Blindness Studies of the Inter-Society Color Council.

For a first-hand view of this truly remarkable development in the field of physiological optics, call your AO Representative.



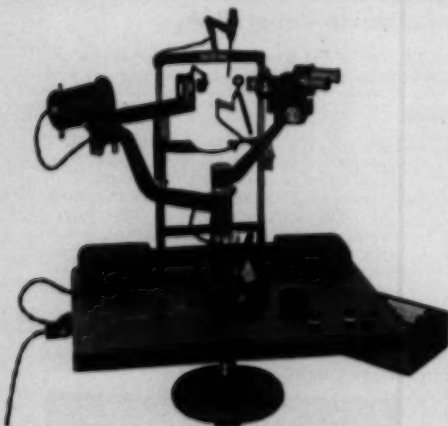
*It is Here:*

## THE BERLINER CATARACT VACUUM PUMP



This perfectly safe and handy instrument has been designed by Dr. Milton L. Berliner, of New York City on the principle of Dr. Barraquer. It has been received with great enthusiasm by many leading surgeons. The amount of suction is easily adjustable to the desired volume. Each instrument is individually constructed and requires practically no maintenance. The metal parts are either aluminum or stainless steel. The instrument is completely silent and vibrationless. AC or DC may be used. Delivered in sturdy, handsome carrying case.

*"Take advantage of our Used Instruments Exchange when buying or selling used equipment of any kind. For information write to address below."*



*Trade in Allowance for Poser and Universal Lamps*

## *The Unique* GOLDMANN SLIT LAMP

- One Arm Control
- Hruby Lens for Fundus Examination
- Many Other Advantages

**U.S. Agents Also for:**

**Perimeters, Ophthalmometers and Other Ophthalmological Equipment.**

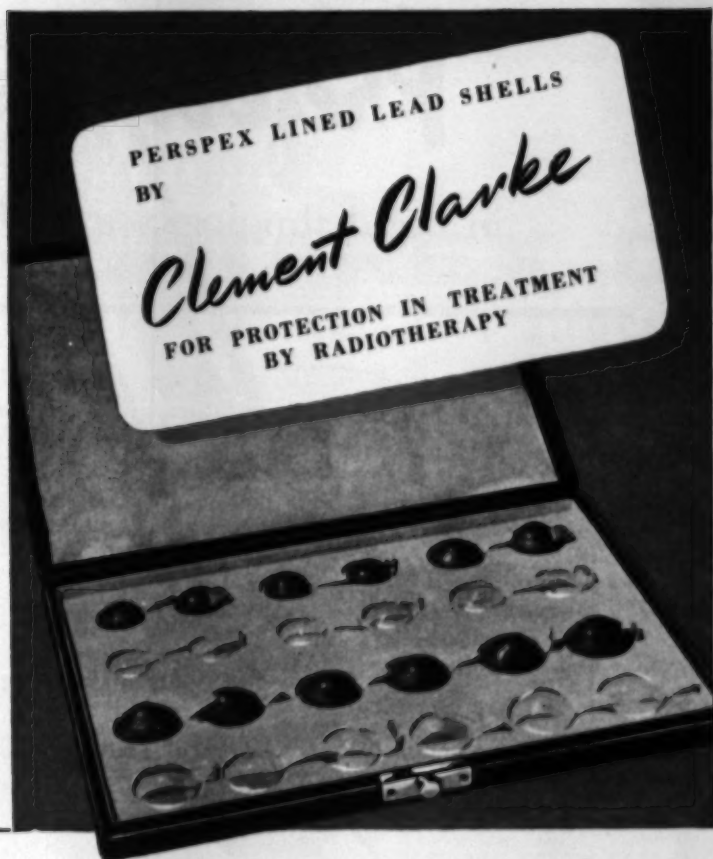
**Can Be Mounted on B & L or AO Stands.**

### ALFRED P. POLL

*Ophthalmic Instruments of Top Quality*  
40 West 55th Street, New York 19, N.Y.



Pat. No. 530108



Perspex lined lead shells in the form of a contact lens afford the eye complete protection when treating parts very close to the eye with X-rays or rays from radio-active substances. By drilling a small hole in the shell it is even possible to carry out localised treatment of a lesion on the sclerotic without exposing the cornea and other parts of the sclerotic to the harmful effects of the radiations. The set of lead shells illustrated comprises six sizes for both right and left eyes. Smaller cases and single shells are also available. *Price, complete in case—\$97.30.*

**CLEMENT CLARKE***of England* • 63 WIGMORE STREET, LONDON, W.1

# Preferred

in ophthalmologic practice

## ISO-SOL®

STERILE OPHTHALMIC SOLUTIONS

- physiologically active
- exceptionally well tolerated
- buffered for stability
- sterile and bacteriostatic

*each dropper bottle is*

- sterile
- tamperproof - sealed
- and dated



**Atropine Sulf.**  
 1/8%, 1%, 2%, 4%  
 for dependable my-  
 driasis and cyclo-  
 plegia.

**Eserine Sal.**  
 1/8%, 1/4%, 1/2%  
 notably effective  
 well tolerated iso-  
 smotic.

**Homatropine HBr.**  
 2%, 3%  
 promptly effective  
 mydriatic isotonic  
 with tears—virtual  
 freedom from side  
 effects.

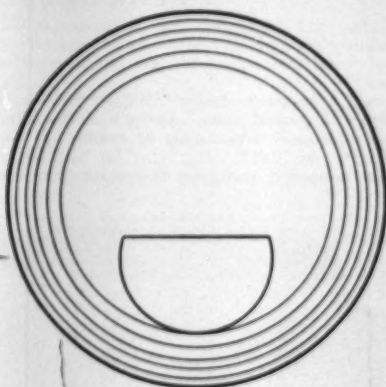
**Pilocarpine HCl.**  
 1/8%, 1%, 2%, 4%  
 effective direct acting  
 non-allergenic  
 buffered.

The ISO-SOL Co., Inc., Brooklyn 17, N.Y.  
 Distributors: Montreal, Panama City

## ISO-SOL®

Write for a descriptive  
 list of all ISO-SOL products.

*In aphakic cases...*  
*after the permanent R<sub>x</sub>*  
*has been established*  
*specify...* **CATAREX 'D'**  
**LENTICULAR CATARACT BIFOCALS**



**For a highly satisfactory  
 post-operative course  
 in cataract cases, use  
 CATAREX temporary  
 cataract bifocals!**

CATAREX Temporary Cataract Bifocals are a revolutionary advance in the field of post-operative aphakic correction, consisting of a 'carrier' lens to which is cemented a spherical bifocal component with straight-top segment. When used in conjunction with CATAREX 'D' permanent lenses, problems of vertex and pupillary distance, segment height and resurfacing are minimized or eliminated entirely because base curves, segment shape and size are identical with those of the permanent CATAREX 'D'. Ask your ophthalmic supplier about this splendid new service!



*For the new brochure,  
 'After Cataract Surgery... Catarex', write...*

The visual ability... and often visual comfort as well... of cataract patients is influenced by the refractionist's choice of a permanent lens. Many times, the weight and distortion of ordinary cataract bifocals have a negative effect on the well-being of the aphakic individual, who must depend upon his lenses to provide vital delineation of detail.

CATAREX 'D' Lenticular Cataract Bifocals were designed to give vastly superior performance over ordinary cataract bifocals in aphakic cases. They are light in weight, cosmetically attractive and yet provide maximum areas in both distance and near fields. Base curve series for CATAREX 'D' number six, with others available on factory order.

**CATAREX 'D' LENTICULAR CATARACT BIFOCALS**

Straight-top segment — 18mm  
 Distance portion — 34mm diameter  
 Standard additions — 2.50D to 3.50D  
 Tint # 1 only

THE  
**VISION-EASE**  
 CORPORATION

Saint Cloud, Minnesota

# VISUAL FIELD EQUIPMENT

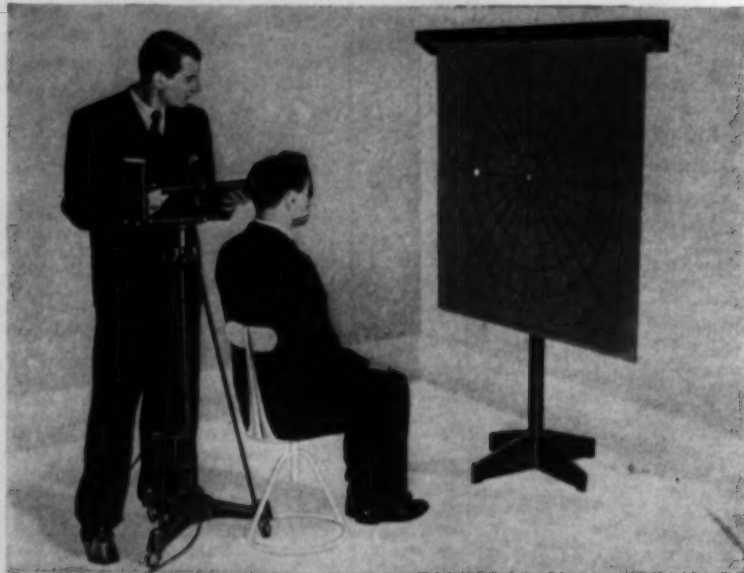
Projection techniques for exploration of the central visual field were pioneered by the KEELER organisation twenty years ago. The original JULER Scotometer, modified to satisfy modern needs, is still unrivalled for accuracy and simplicity. It gives reliable scotoma records\* for cases that are difficult or impossible with conventional Test Objects and black tangent screen.



JULER HAND SCOTOMETER

## FEATURES

- Stimuli, projected onto the Keeler One- or two-meter GREY Bjerrum screen, can be changed rapidly and silently by finger-tip control of colour and size (1 to 30mm).
- Elimination of wand and pauses for test object interchange helps patient's concentration—lessens fatigue.
- Powerful 12watt. light gives adequate contrast between stimulus and screen luminance—permits higher level of general room lighting than has hitherto been possible.
- Marking pins, subsequent transcribing of results, are abolished, as operator can hold Scotometer and chart in one hand, using other for marking the scotomata.
- As no assistant is needed, the Juler Scotometer cuts costs, saves time and gives greater accuracy.



## AUTOMATIC RECORDING MODEL WITH GREY BJERRUM SCREEN

Incorporating Juler Scotometer on universal joint to ensure maximum efficiency by means of convenient foot-controlled automatic recorder. The Grey Bjerrum screens by Keeler are specially designed for optimum results with the Juler Scotometer. They are available as portable stand models (as shown) or wall-fixing models. Also available in black.

\* Am. J. Ophth. 36, 1130, 1953 Br. J. Ophth. 1939, 23, 239.

**KEELER OPTICAL PRODUCTS, INC.**

617 S. 52nd St., Philadelphia 43, Pa., U.S.A.

Telephones: GRANITE 4-5310 & KINGSWOOD 4-0874

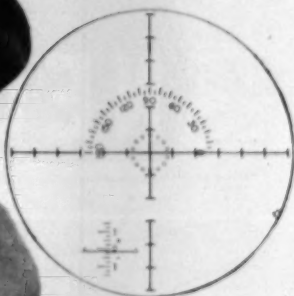


OPTICAL INSTRUMENTS



SINCE 1857, GOTTINGEN, ALLIED ZONE

# VERTEX REFRACTIONOMETER



A small, sturdy, well-balanced instrument ideally suited for the ophthalmologist's office and optician's shop. Can be easily operated by nurses, secretaries, or optical craftsmen.

- Convenient and exact readings at a glance.
- Even small cylinders can be easily detected and accurately measured.
- Target image as well as refraction scale seen in the same field of view.
- Built-in illumination. Fully dustproof.
- Guaranteed uninterrupted repair service.

**MADE IN WEST GERMANY**

*Write for detailed literature and specifications*

**CARL ZEISS, INC.,** 485 Fifth Avenue, New York 17, N.Y.



# A TIME TESTED FORMULA IN OPHTHALMOLOGY



BURK OPTIC®  
**NEOZIN**

**STERILE**  
*Buffered*  
**OPHTHALMIC SOLUTION**

## NEW PLASTIC CONTAINER

- Easy to Carry
- Convenient to Use
- Will not break or spill.

### FORMULA

Neo-Synephine\*Hydrochloride ..... ½ %  
Zinc Sulfate ..... ½ gr. (0.032 gm.)  
Zephiran\* chloride ..... 1:25,000

In a non-irritating STERILE buffered aqueous solution.

NEOZIN is the Trademark of  
Professional Pharmacal Co., Inc.  
\*Registered Trademark of  
Wintrop-Stearns, Inc.

NEOZIN'S astringent, antiseptic and decongestant action is particularly effective in catarhal, allergic, or inflammatory conjunctivitis. NEOZIN relieves itching and smarting associated with eyestrain, and provides the gentle, soothing effect desired in treating ocular inflammation. May be used with safety in all age groups.

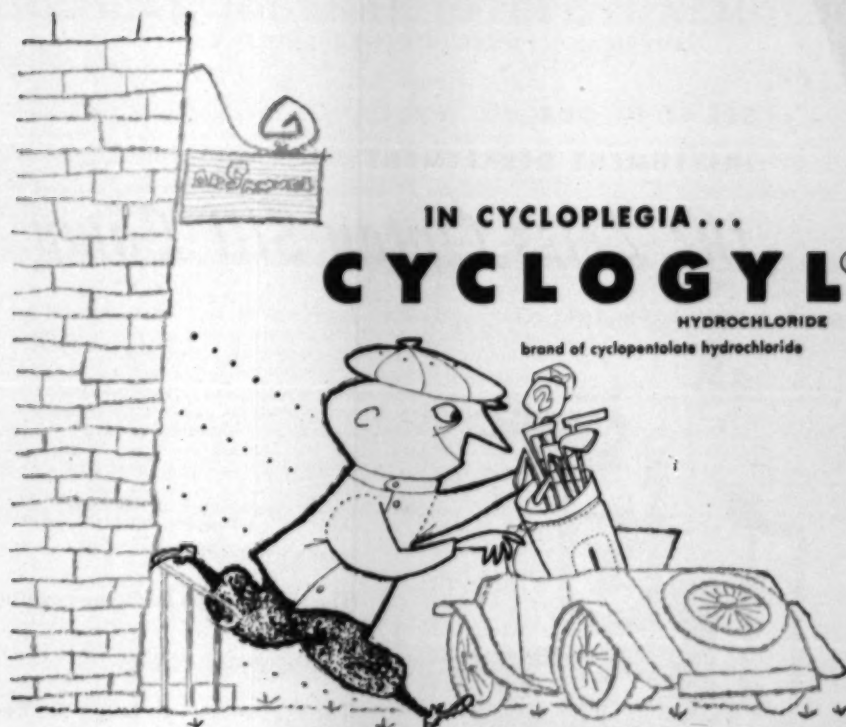
Supplied in new 15cc. PLASTIC container, and in hermetically sealed 15cc. glass vial, dropper enclosed.

WRITE FOR SAMPLES & LITERATURE

*"It Meets the Eye Without Protest"*

Professional Pharmacal Co., Inc.

Pharmaceutical Manufacturers San Antonio, Texas



# IN CYCLOPLEGIA... **CYCLOGYL®**

HYDROCHLORIDE

brand of cyclopentolate hydrochloride

## **SAVES TIME**

... for you ... with rapid onset of action  
... for your patients ... with rapid recovery

"Cyclopentolate hydrochloride ... produces a rapid [30 to 60 minutes], intense cycloplegia and mydriasis of moderate duration ... and is effective in highly pigmented irises and for persons of all ages."

*New and Nonofficial Remedies, Philadelphia, J. B. Lippincott Company, 1954, p. 189.*

Cyclogyl has shown outstanding qualities in 1035 cases.<sup>1</sup>  
(Incorporates work of 11 previous investigators)

Compound	Dosage and Administration (drops) *	Diopeters of Residual Accommodation	Spontaneous Recovery (in hours)
Cyclogyl 0.5%	2	1.10	24†
Homatropine 2% or 4%	2	2.00	48

\* Successive drops at five-minute intervals.

† Recovery time reduced to six hours after one-percent pilocarpine.

*1. Gordon, D. M., and Ehrenberg, M. H.: Am. J. Ophth. 38:831 (Dec.) 1954.*

"the chief handicap of maximum cycloplegia, namely its incapacitating effect, is minimized ..."

*Gunn, B. C.: A.M.A. Arch. Ophth. 51:467 (Apr.) 1954.*

Cyclogyl, "by virtue of its brevity, rapidity of action, and consistent depth of cycloplegia, will be [a drug of choice] for routine refraction ..."

*Ehrlich, L. H.: New York J. Med. 55:3015 (Dec. 15) 1955.*

### Dosage:

Cycloplegia - One drop 1.0%, in each eye (or two drops of 0.5%) produces maximal cycloplegia in 30-60 minutes. Recovery time is normally 4-12 hours spontaneously. Pilocarpine reduces recovery time. In deeply pigmented eyes, 2 drops of 1.0% in each eye, instilled 10 minutes apart, achieves satisfactory cycloplegia in 98% of cases.

Mydriasis - One or two drops of 0.5% in each eye.

Samples and Literature on request.

### Supplied:

Sterile ophthalmic solution in Gifford's Buffer (pH 6.0)  
0.5% Solution - 15 cc Dropper Bottles  
1.0% Solution - 15 cc Dropper Bottles  
2 cc Dropper Bottles



**Schiffelin & Co.** Since 1794

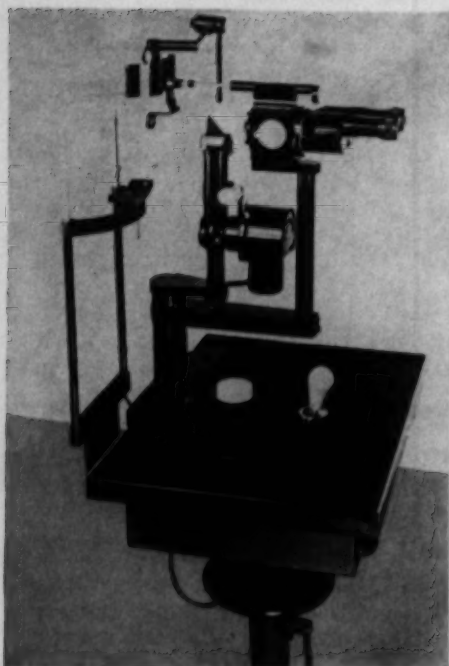
Pharmaceutical and Research Laboratories  
New York 3, N. Y.

XVIII  
DOCTOR,

AMERICAN JOURNAL OF OPHTHALMOLOGY

SEE IT IN OUR  
INSTRUMENT DEPARTMENT—

## *the Zeiss Opton Slit Lamp*



This slit lamp requires no adjustments whatsoever.

The slit lamp can be swung past the corneal microscope without interruption of observation.

The microscope can be set for five different magnifications solely by turning a knob without a change of oculars or objectives.

The working distance remains the same for all magnifications.

A supplementary attachment permits, in an optically correct and manually simple fashion, slit lamp

microscopy of the deep vitreous—and binocular ophthalmoscopy in either white or red-free light.

All manipulative parts are positioned to facilitate quick and satisfying use of the instrument.

A fine optical instrument by Zeiss—a great name in optics.

*Also available with compound stage to fit deluxe floor stand.*

### *The House of Vision Inc.*

30 NORTH MICHIGAN AVENUE, CHICAGO  
MILWAUKEE • MINNEAPOLIS • DES MOINES

# AMERICAN JOURNAL OF OPHTHALMOLOGY

SERIES 3

VOLUME 39

NUMBER 5

MAY, 1955

## CONTENTS

### COLOR PLATE

Illustrating paper by Charles L. Schepens .....	facing page 631
---	-----------------

### ORIGINAL ARTICLES

Fundus changes caused by alterations of the vitreous body. Charles L. Schepens .....	631
Tapetoretinal degeneration of late onset. J. François and G. Decock .....	633
Hereditary degeneration of the macula: Occurring in five generations. C. Truman Davis and Robert W. Hollenhorst .....	637
Congenital retinal fold: A case report. Stefan Van Wien and William B. Sullivan .....	643
Macular holes in retinal separations: Their significance and their surgery. Arthur H. Keeney .....	648
Effective treatment of tuberculous choroiditis. James E. Lebensohn .....	653
Calcified scleral nodules in hypervitaminosis D. Samuel Gartner and Karl Rubner .....	658
Tuberous sclerosis: Historical review and report of two cases. William Joachim Pagenstecher .....	663
Vitreous hemorrhage absorption: Experimental study on rabbit eyes of the effects of intravitreal hyaluronidase and streptokinase-streptodornase and on the influence of ACTH and cortisone. R. A. Schimek and E. H. Steffensen .....	677
Mechanism of miopiesin formation. Ernst Schmerl, Albert A. Dietz and Bernhard Steinberg .....	684
The effect of the broad and medium spectrum antibiotics on the virus of herpes simplex. Ruth G. MacKneson and H. L. Ormsby .....	689
Laboratory observations on the ocular use of tetracycline. J. W. Hallett, Khalida Naib and Irving H. Leopold .....	691
Simplified method of curare administration in cataract surgery. Oscar Dahlene and J. Wesley McKinney .....	697
Influence of coffee upon ocular tension: In normal and glaucomatous eyes. W. Leydhecker ..	700
Flicker-fusion frequency and hypertension. Jordan M. Scher and Willard H. Spankus .....	705
The cataract operation as an office procedure. Lyndon Evelyn .....	715
Objective methods of refraction: A comparison of the Rodenstock eye-refractometer and the Reid streak-retinoscope in determining the refractive status of an eye. David Volk .....	719

### NOTES, CASES, INSTRUMENTS

A case of syringomyelia: Associated with vascular anomalies of the eyes. Norman Yourish, Nathaniel Wollin and Arthur Nathaniel .....	728
Streptokinase and streptodornase: In intraocular hemorrhage. Arthur Sacks-Wilner, S. Sinclair and Truman Boyes .....	730
Congenital neuroparalytic keratitis. Walter Segall .....	732
Altitudinal hemianopsia and papilledema. B. G. Prater and Robert L. Lam .....	738

### SOCIETY PROCEEDINGS

Chicago Ophthalmological Society, January 18, 1954 .....	742
Ophthalmological Society of Madrid, April 22, 1954 .....	744
Memphis Eye, Ear, Nose, and Throat Society .....	745
Yale University Clinical Conference, January 29, 1954 .....	749
New York Society for Clinical Ophthalmology, March 1, 1954 .....	752
College of Physicians of Philadelphia, Section on Ophthalmology, February 18, 1954 .....	757

### EDITORIALS

The chemotherapy of eye tuberculosis .....	758
Wills Eye Hospital: Seventh Annual Clinical Conference .....	759

### OBITUARIES

George H. Cross .....	762
Stephen L. Polyak .....	762

### CORRESPONDENCE

Request for nonmagnetic foreign bodies .....	763
Beta radiation therapy .....	764

### BOOK REVIEWS

Viral and Rickettsial Diseases of the Skin, Eye, and Mucous Membranes of Man .....	766
Current Therapy 1955 .....	766
Human Physiology .....	767
Hydrostatics and Hydrodynamics of the Eye .....	767
Hundredth Year Celebration of the Birth of Paul Ehrlich and Emil v. Behring .....	768
Hyperostosis Cranii .....	768
Neuro-ophthalmology .....	769
Books received for review .....	769

### ABSTRACTS

Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous; Neuro-ophthalmology; Eyeball, orbit, sinuses; Eyelids, lacrimal apparatus; Tumors; Systemic disease and parasites .....	770
---	-----

### NEWS ITEMS

789



A balanced combination of  
decongestant, astringent and antiseptic,  
OpH promptly soothes  
minor ocular irritations.

OpH is sterile,  
buffered and  
isotonic with tears.

**OpH formula:**

Neo-Synephrine® hydrochloride (0.08%)  
zinc sulfate (0.06%)  
boric acid (2.2%).

Supplied in new, handy individual dropper bottles  
(10 cc.) which prevent dropper contamination.

Specify-OpH-new sanitary ophthalmic preparation  
in prescription type package.

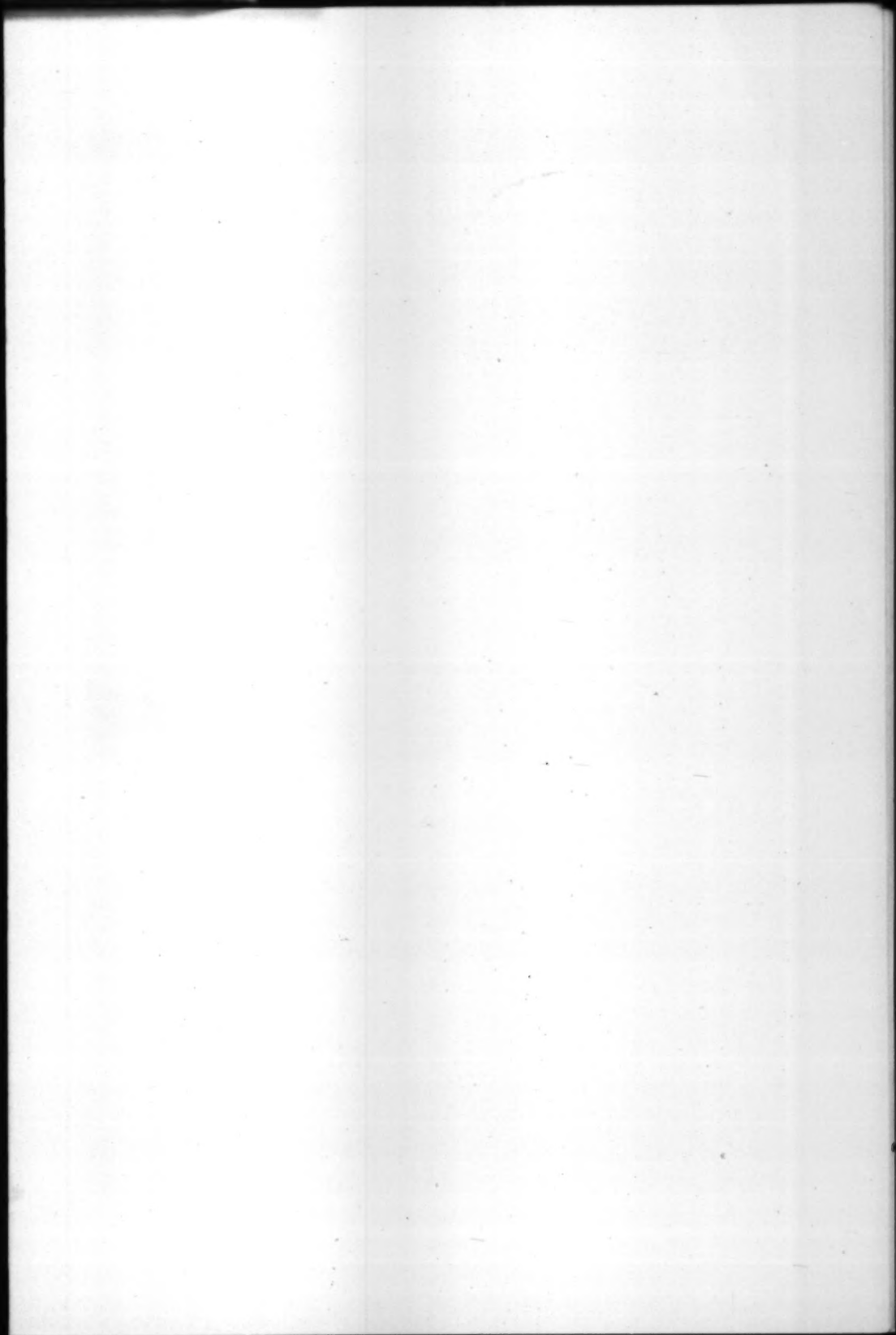


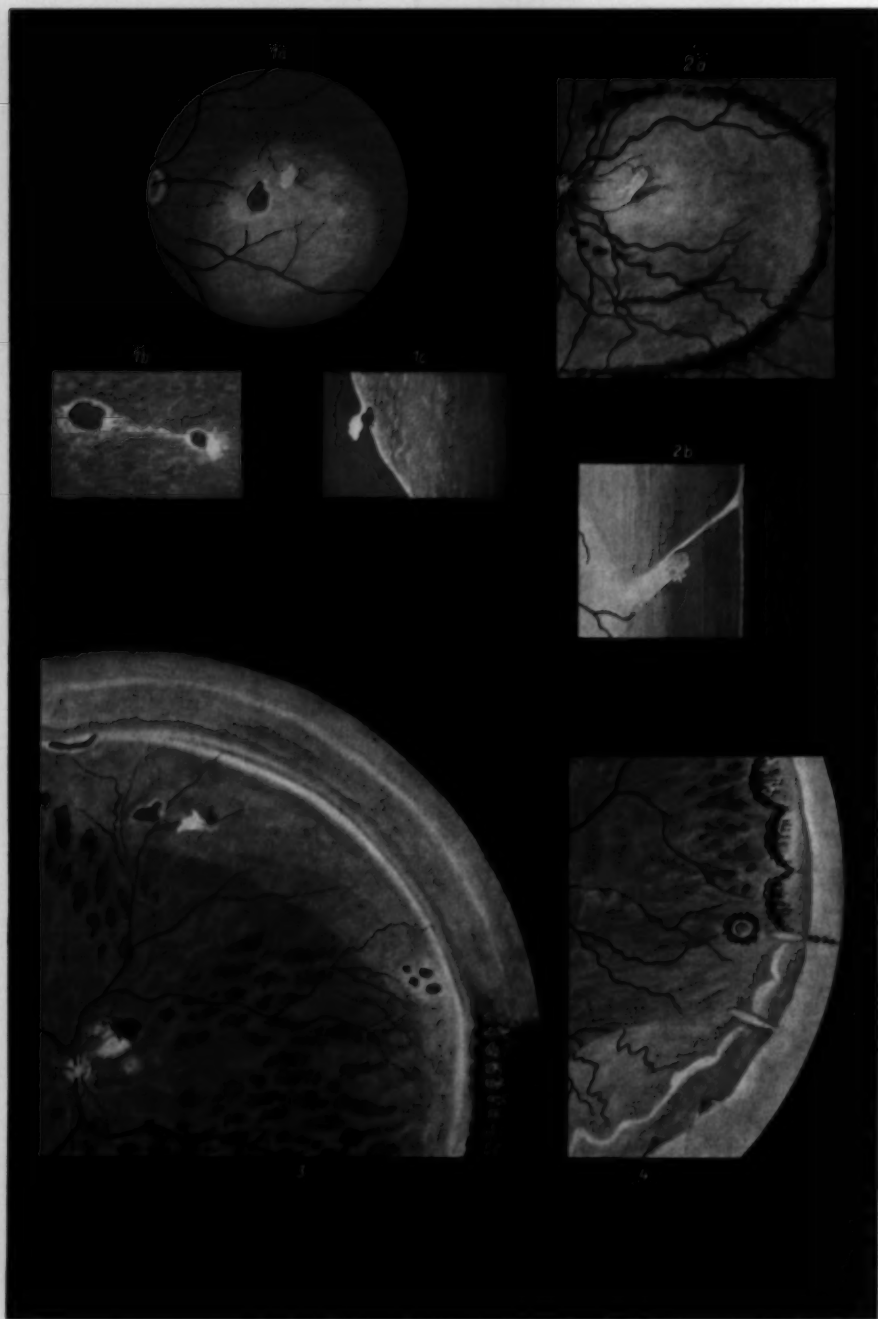
**WINTHROP-STEARNES INC.** New York 18, N. Y. • Windsor, Ont.

Neo-Synephrine (brand of phenylephrine), trademark reg. U. S. & Canada

Visit our Booths #B 12-14 and C 11-13  
A.M.A. Convention, June 6-10, 1955







Figs. 1a, 1b, 1c, 2a, 2b, 3, and 4 (Schepens), Fundus changes caused by alterations of the vitreous body.

# AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 39

MAY, 1955

NUMBER 5

## FUNDUS CHANGES CAUSED BY ALTERATIONS OF THE VITREOUS BODY\*

CHARLES L. SCHEPENS, M.D.

Boston, Massachusetts

In a previous publication,<sup>†</sup> clinical aspects of changes in the vitreous body have been discussed in some detail. The purpose of this paper is to illustrate, by examples, alterations in the macula and ora serrata caused by the vitreous body.

### MACULAR CHANGES

In two cases, remarkable alterations in the macula were probably caused by detachment of the hyaloid membrane from the region of the posterior pole.

#### CASE 1

A man, aged 57 years, complained that, in three months' time, vision in the left eye had gradually deteriorated from 20/20 to 20/200.

\* From the Retina Service and Retina Foundation, Department of Ophthalmology of the Massachusetts Eye and Ear Infirmary and Harvard Medical School. (Paper 18, Retina Foundation and Retina Service.) This work was supported by the Institute of Neurological Diseases and Blindness, of the National Institutes of Health, Department of Health, Education, and Welfare (Grant No. B56R and No. B56C), by the Vivian B. Allen Foundation, and by the American Optical Company.

† Schepens, C. L.: Clinical aspects of pathologic changes in the vitreous body. *Am. J. Ophth.*, **38**: 1-21 (July, Part II) 1954.

When first examined, macular edema was noticed but, a few weeks later, a true macular tear surrounded by flat retinal detachment was observed.

In Figure 1a, the tear is somewhat irregular, about half the size of the disc, and an operculum is present on its temporal side, casting a shadow on the detached retina.

Examination with the slitlamp and flat contact lens reveals the presence of a fine membrane located in the vitreous cavity, in front of the disc and macula (fig. 1b). This picture is obtained by focusing the slitlamp microscope on the membrane and then sweeping the "joy-stick"<sup>‡</sup> laterally.

An annular thickening of the membrane surrounds a hole which corresponds to the area of the disc. Temporally, the annular thickening is continuous with a dense band, at the end of which another annular thickening is visible. The latter surrounds a smaller hole, which is located in front of the macula.

When an optical section is carefully examined (fig. 1c), it is apparent that, posterior to the limiting membrane, the vitreous cavity

‡ A "joy-stick" arrangement is found in the Haag-Streit, the Zeiss-Opton, or the Aimark slitlamps.

Figs. 1a, 1b, and 1c. Macular detachment probably due to traction by the hyaloid membrane (W. C. Retina Service No. 1982).

(1a) Ophthalmoscopic view of the macular detachment, with tear and operculum.

(1b) Composite slitlamp view of the membrane located in the vitreous cavity, in front of the disc and macula.

(1c) Slitlamp view (light at the observer's right) of the limiting membrane, with central hole, and operculum attached posteriorly.

Figs. 2a and 2b. Macular detachment without visible break, probably due to traction by the hyaloid membrane upon the normal vitreoretinal adhesions present in the macular region (L. H. Retina Service No. 989).

(2a) Ophthalmoscopic view; note the demarcation line.

(2b) Composite slitlamp view (light at observer's right) showing the traction band between the limiting membrane and the macular area.

Fig. 3. Fundus view of the upper temporal quadrant in a case showing paracentral choriorretinitis and peripheral retinal detachment. The ora serrata is extensively detached (A. C. Retina Service No. 1129).

Fig. 4. Portion of the nasal fundus in a case with inferior retinal detachment. The ora serrata is detached below and breaks are present in the pars plana ciliaris (B. K. Retina Service No. 1754).

ity is optically empty; whereas, anteriorly, vitreous gel is present. The operculum is attached to the posterior face of the limiting membrane, on the edge of the smaller hole.

Examination of the patient's right eye showed a vision of 20/20 and a so-called vitreous detachment with a hole in the posterior limiting membrane, in front of the disc.

#### CASE 2

A man, aged 68 years, had developed a central scotoma in the left eye, one year previously. As the macula appeared normal at the time, a tentative diagnosis of retrobulbar neuritis was made. Then, in the course of a few months, he gradually developed an unusual fundus picture.

As seen in Figure 2a, a smooth and central retinal detachment is present; it is limited by a curved demarcation line. The detachment is dome-shaped, with a tubular elevation, two to three-mm. long, in the area of the macula. Below the macula, and behind the detached retina, there are two incomplete pigmented demarcation lines in the choroid, which have been broken through by the retinal detachment.

Figure 2b is a composite picture of the slitlamp appearance. The dome-shaped retinal detachment is well visible. The macula forms a small red dot surrounded by a yellow area, close to the tip of the tubular elevation. A coarse strand connects the tubular elevation with a taut membrane, stretched along the equatorial plane of the vitreous cavity. Under the insertion of the strand, on the tubular elevation, there are whitish pieces of tissue which hang into the vitreous cavity. The space between the retina and the smooth membrane appears optically empty, whereas the space anterior to the membrane contains vitreous gel.

It is probable that the taut membrane is the hyaloid and that one deals with a true vitreous detachment. The coarse strand connecting the hyaloid membrane to a point located above the macula is probably one of

the normal adhesions of the hyaloid to the macular area. This adhesion has stretched considerably, whereas the small pieces of tissue seen hanging below the macula are probably ruptured adhesions.

No abnormality was detected in the patient's other eye.

#### CHANGES AT THE ORA SERRATA

A careful study of the region of the ora serrata with an indirect stereoscopic ophthalmoscope may reveal details concerning the anatomic relationships between the vitreous body and the peripheral retina. The following two cases are examples of interest.

#### CASE 1

A man, aged 24 years, was treated for a well-visible focus of paracentral chorioretinitis, located above the disc and macula in the left eye; the right eye showed no abnormality. Upon routine examination of the left fundus periphery, a small retinal detachment was found.

One retinal break is visible at the 12-o'clock position, one at the 12:30-o'clock position, and two at the 2:30-o'clock position (fig. 3). At the 1-o'clock position, an operculum shows visible vitreous fibers attached to its internal side. The retinohoroidal adhesion, which is normally present at the ora serrata, is detached from the 11-o'clock to about the 3-o'clock position. The ciliary epithelium, which covers the pars plana ciliaris in this area, is detached from the pigment epithelium, and this detachment casts a haze over the underlying choroid. A retinal fold, parallel and slightly posterior to the ora serrata, extends along the whole area represented in this picture; a second fold, in the middle of the pars plana ciliaris, runs from the 11-o'clock to the 2:30-o'clock position.

This fundus picture is explained by the rupture of the retinohoroidal adhesion which is normally present at the ora serrata. As a result, the retinal detachment has extended into the pars plana ciliaris. Such an

observation is more unusual on the temporal side of the ora serrata than on the nasal side, because the retinochoroidal adhesion is broader and stronger temporally than nasally.

The retinal fold, located at the posterior border of the ora serrata, probably coincides with the posterior border of the vitreo-retinal symphysis, whereas, the fold in the middle of the pars plana ciliaris corresponds approximately with the anterior border of the symphysis. It is probable that this type of condition is caused by traction exerted on the vitreo-retinal symphysis by the vitreous body.

#### CASE 2

A woman, aged 43 years, had a bilateral uncomplicated intracapsular cataract extraction four years previously. Vision with the right eye had been poor for one year due to an inferior retinal detachment. The left eye had good vision and revealed no remarkable abnormalities.

Figure 4 represents a portion of the nasal fundus periphery in the right eye. Normal ora serrata is visible above; below, the choroidal pigmentation, corresponding to the scallops of the ora serrata, is hidden by the detached retina. The latter has been torn

loose from its attachment to the choroid. As a result, the retinal detachment has extended under the ciliary epithelium. In this region, two wavy grayish lines are visible: an anterior line caused by a fold in the ciliary epithelium, and a posterior line which is the ora serrata.

Other details of interest should be noted:

Two meridional folds are present between the 3-o'clock and 4-o'clock positions; close to the ora serrata, there is a circular pigmented chorioretinal adhesion, inside of which a minute retinal detachment surrounds a round break in the retina; two other breaks are located in the ciliary epithelium, between the 4-o'clock and 5-o'clock positions, bordering the fold in this area.

In this case, also, detachment of the ora serrata from the underlying choroid is probably the result of traction on the vitreo-retinal symphysis by the vitreous body. This mechanism explains the tears in the ciliary epithelium and the two parallel folds, each one of which corresponds to one border of the symphysis. It is likely that the meridional folds result from the fact that, on the nasal side, the retinochoroidal attachment is scalloped.

243 Charles Street (14).

### TAPETORETINAL DEGENERATION OF LATE ONSET\*

J. FRANÇOIS, M.D., AND G. DECOCK, M.D.  
*Ghent, Belgium*

We think that it may be of interest to report two cases of tapetoretinal degeneration in which the onset was at a particularly advanced age and in which the evolution was markedly similar.

#### CASE 1

H. L., aged 71 years, was first seen in 1951, complaining of diminished vision which

had begun three years previously. He complained also of not being able to move about without knocking into obstacles in his way.

The vision was still 4/10 in the right eye and 6/10 in the left, but there was on both sides a concentric contraction of the visual field to 10 degrees.

Although the anterior segment of the eyes did not present any anomaly, the fundus showed a pale disc with slightly blurred margins; the retinal arteries and veins were

\*From the Ophthalmological Clinic of the University of Ghent.



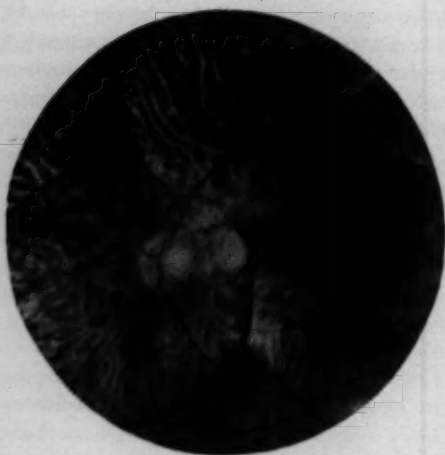


Fig. 1 (François and Decock). Case 1.  
Appearance of fundus.

very fine and disappeared in the periphery.

Later the central vision continued to diminish progressively and, in February, 1954, the following observations were made:

The anterior segment was normal. The pupils were equal and their reflexes brisk both for light and for convergence. The lens presented a diffuse cloudiness more pronounced on the right than on the left.

*Ophthalmoscopy* (fig. 1) showed on both sides a dirty white disc but with clearly defined limits. The retinal vessels were extremely fine, filiform in fact; only the tem-

poral vessels could be followed for a distance of four disc diameters. The retina seemed to be avascular beyond the posterior pole, as though the arterial as well as the venous network was atrophied. The macular region presented a homogeneous aspect of a brownish color without evident alterations. There was an atrophy of the pigmentary epithelium, leaving visible the clearly sclerosed choroidal vessels (diffuse choroidal sclerosis); at the level of the superior internal quadrant of the retina, on both sides, several smallish pigmentary masses were found.

*Ocular tension* was normal in both eyes. There was no anomaly of the ocular musculature or the adnexa.

*Visual acuity* was 1/20, right, and 4/10 left. The visual field (fig. 2) was concentrically contracted to five degrees on both sides (Goldmann's perimeter: tests 4/5 and 4/3).

The *adaptation curve* (fig. 3) was clearly abnormal; it was spread out horizontally to the extent that even after half an hour there was not the least adaptation.

The *electroretinogram* (fig. 4) showed a complete absence of retinal response.

The *electroencephalogram* of low voltage presented a dominant alpha rhythm, not, on the whole very regular, of 11 to 12 c.s., reaching 15 to 25  $\mu$ V and presenting a rapid component in all derivations. In the occipital and temporo-occipital regions slow waves of

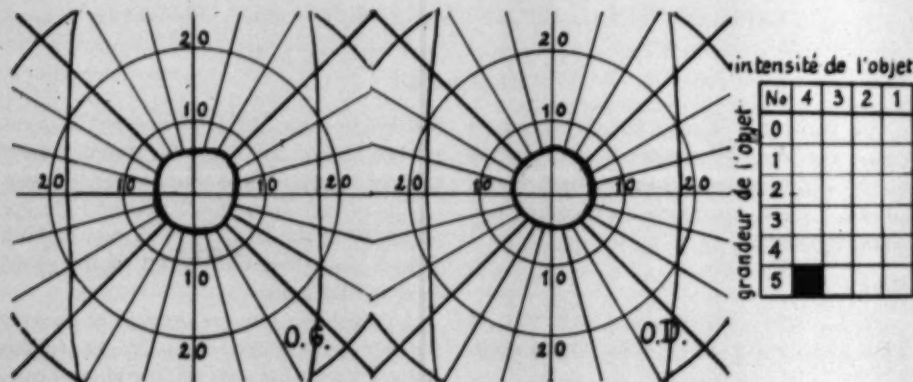


Fig. 2 (François and Decock). Case 1. The visual field.

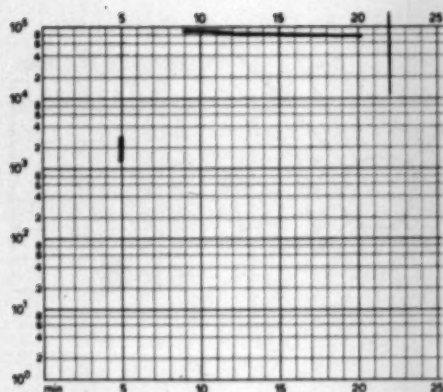


Fig. 3 (François and Decock). Case 1.  
The adaptation curve.

4 to 6 c.s., were found; spike waves were also registered, especially in the temporal and parieto-occipital regions. No signs of focalization was present. The blocking reaction was hardly noticeable. The record was little modified by hyperpnea.

The otologic examination showed a bilateral tympanosclerosis. Audiometry gave the classic curve of a presbycusis in accord with the age of the patient.

A thorough general examination did not give any particular information. The Bordet-Wassermann reaction was negative. No similar case existed in the family. The patient has had no serious infectious illness.

#### CASE 2

B. P., aged 65 years, came in October, 1953, complaining that he bumped against obstacles in his way. The first difficulties had commenced three years before. The visual acuity was still 10/10 for each eye.

In February, 1954, we were able to make the following observations:

The anterior segment was normal. The pupils were equal but their reflexes were slow and of small amplitude. The lens showed a slight diffuse cloudiness.

*Ophthalmoscopy* (fig. 5) showed discs of a chamois color with indistinct borders. The retinal vessels were very fine and ramified.

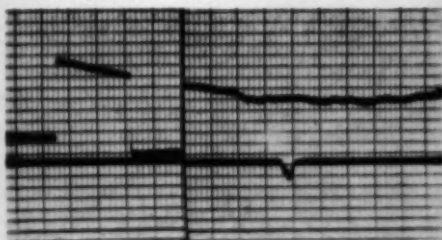


Fig. 4 (François and Decock). Case 1.  
The electroretinogram.

The vascular tree seemed to be reduced to its principal branches. The macula was dappled and of a brownish color. The periphery of the retina presented a "pepper-and-salt" aspect. The choroidal vessels which were visible here and there were sclerosed. There were no osteoclasts but, at the level of the superior nasal quadrant of the two eyes, several smallish pigmentary masses were found.

*The ocular tension* was normal in both eyes. There was no anomaly of the ocular musculature or of the adnexa.

*The visual acuity* was 7/10, right, and 8/10 left. The visual field (fig. 6) was concentrically reduced to five degrees on both sides (Goldmann perimeter: tests 4/5 and 4/3).

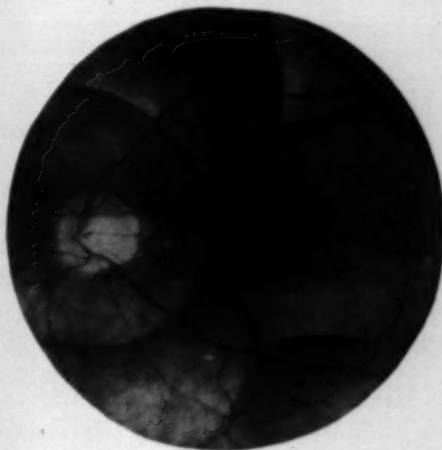


Fig. 5 (François and Decock). Case 2.  
Appearance of the fundus.

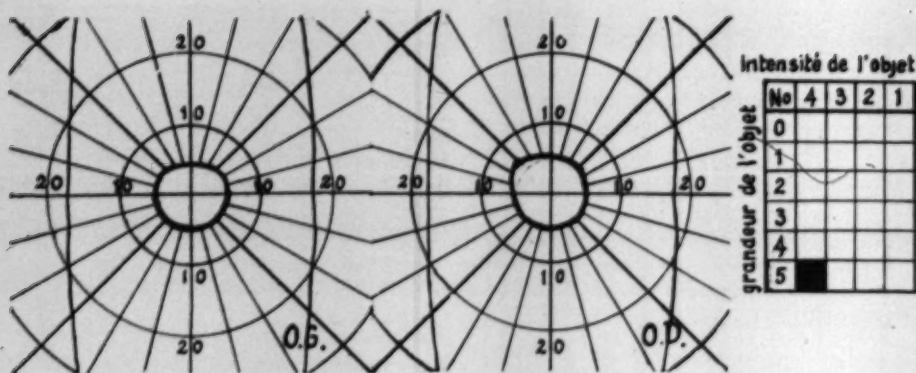


Fig. 6 (François and Decock). Case 2. The visual field.

The adaptation curve (fig. 7) was clearly retarded.

The electroretinogram (fig. 8) did not show any retinal response.

The electroencephalogram contained an alpha rhythm of 8 c.s., fairly regular on the whole, abundant in all the derivations, reaching 30 to 40  $\mu$ V and symmetric in both hemispheres. The basic rhythm also presented rapid rhythms at 18 to 24 c.s. The blocking reaction was little in evidence. The hyperpnea did not show on the record but, toward the end, small puffs of alpha waves appeared. They were of high voltage, taking at times the appearance of spike waves. To sum up, there was seen, then, a record of low voltage, presenting a regular and symmetric alpha rhythm, which must be considered as normal.

The otologic examination showed normal

drums. Audiometry gave a bilateral presbycusis deficiency curve in accord with the patient's age.

A thorough general examination gave no particular information. The Bordet-Wassermann reaction was negative. There had been no other similar case in the family. The patient had had no serious infectious illness.

#### DISCUSSION

The ophthalmoscopic examination (discs of a chamois color, filiform vessels, retinal atrophy, and choroidal sclerosis), the functional examination (concentric shrinking of the visual field to five degrees), the absence of electroretinographic response, and insufficient or no adaptation are sufficient proof that tapetoretinal degeneration is present in our two patients. Indeed, in one case the electroencephalographic record was identical

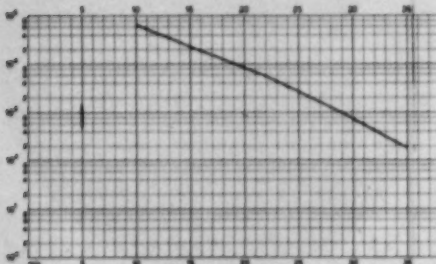


Fig. 7 (François and Decock). Case 2. The adaptation curve.

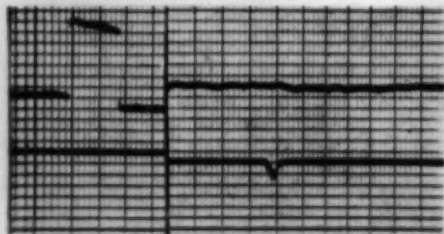


Fig. 8 (François and Decock). Case 2. The electroretinogram.

to that found in most cases of pigmentary retinopathy.

The interest of these two cases lies above all in the fact that the affection was of a very late onset, at 65 years of age in one case, at 62 years of age in the other.

Further, the following salient points should be emphasized:

1. The evolution of the tapetoretinal degeneration, identical in both cases, was very rapid—in three years there was a concentric shrinking of the visual field to five or ten degrees.

2. There is no parallelism between the loss of central vision and that of peripheral vision; our second patient still has a visual acuity of 7/10 in one eye and 8/10 in the other, although the visual field is already concentrically reduced to five degrees.

3. One does not find, at the level of the eye fundus, the typical pigment deposits of pigmentary retinopathy. The tapetoretinal degeneration in our two cases is characterized by a simple retinal atrophy with chorioidal sclerosis.

4. In each case the patient is the only afflicted individual in a family otherwise completely normal.

#### SUMMARY

Two cases of tapetoretinal degeneration have been reported. They were characterized by a late onset, by rapid evolution, and by absence of a parallelism between the loss of central vision, relatively well preserved, and the loss of peripheral vision, completely lost.

*Pasteurlaan 2.*

## HEREDITARY DEGENERATION OF THE MACULA\*

OCCURRING IN FIVE GENERATIONS

C. TRUMAN DAVIS,<sup>†</sup> M.D.

AND

ROBERT W. HOLLENHORST,<sup>‡</sup> M.D.

*Rochester, Minnesota*

Heredofamilial degeneration of the macula lutea without cerebral complications is a comparatively rare disease of which the true etiology and pathogenesis are unknown and for which no treatment is known at the time of this study.

The affection was first reported in 1897 in England by Batten,<sup>1</sup> who described a famil-

ial form involving the eyes of two brothers whose father and mother were free of the disease. In 1905, Best<sup>2</sup> reported the cases of various members of the same family who had hereditary degeneration of the retina in which the lesion was inferior to the macula of each eye. Since his reports, this family has been studied extensively by others. In 1909, Stargardt<sup>3</sup> reported several cases in which siblings were affected with macular degeneration. None of these patients knew of parents or other ancestors who had the disease.

In 1920, Behr<sup>4</sup> presented 16 cases of familial macular degeneration to which six families were affected. In each family the patient's age at onset of the disease was

\*Abridgment of thesis submitted by Dr. Davis to the faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Ophthalmology.

<sup>†</sup>Fellow in Ophthalmology, Mayo Foundation. The Mayo Foundation in Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

<sup>‡</sup>Section of Ophthalmology, Mayo Clinic and Mayo Foundation.



typical. In some cases a definite hereditary pattern was noted; that is, several members of three generations were involved. Behr classified the disease by the age of the patient at onset into infantile, adolescent, young adult, presenile, and senile types. This method is not entirely satisfactory but is the one in general use today. Behr also gave an excellent description of the subjective complaints associated with the various lesions.

In 1940, Sorsby<sup>8</sup> cleared up much of the confusion which had previously existed in the classification of familial and hereditary degenerative conditions in and about the macula by presenting a clear and concise classification based on the clinical course and morphology of the lesions. In this classification Sorsby includes: (1) Congenital coloboma of the macula, (2) Best's disease (familial paramacular involvement with usually good vision), (3) macular dystrophy (true macular degeneration of the hereditary type without cerebral involvement), (4) Doyne's choroiditis, (5) angioid streaks, and (6) central choroidal sclerosis.

Several papers on familial degeneration of the macula have been presented during the last 10 years. Crawford<sup>6</sup> reviewed the literature and in addition reported eight cases of the disease among four separate families. In all of these cases the parents were free of the disease. Falls<sup>7</sup> reported six cases of the disease with unbroken dominant transmission in three generations. Berkley and Bussey<sup>8</sup> described eight cases with a dominant hereditary transfer which had imperfect penetration. Mortelmans,<sup>9</sup> in 1950, reported the cases of three brothers in whom a form of progressive macular degeneration developed after injuries to the head.

In 1950, Klien<sup>10</sup> reviewed the subject and presented the pathologic aspects in a case in which macular degeneration had developed when the patient was 57 years of age. She made no mention of a similar affection of siblings or parents. In 1951, Sun<sup>11</sup> reported a case of bilateral macular degenera-

tion in a Chinese patient. There is no history of involvement of this patient's parents, siblings, or offspring.

#### REPORT OF CASES

In our study we found progressive symmetrically bilateral degeneration of the maculas in 24 persons belonging to the same family, which consisted of 148 members and represented five generations. This family was discovered when two young women, 29-year-old first cousins, presented themselves for examination at the Mayo Clinic because of progressive loss of visual acuity in each eye since early childhood. The case of one of these patients is reported herein (Case 1).

The visual defects in each of these two young women were identical. As they were questioned the existence of many similar visual defects among their kin was disclosed.

Since virtually the entire family resided in central Wisconsin, it was possible to make a complete genetic study. With the few exceptions noted in Figure 1 the entire family could be examined in detail. It was soon evident that a macular lesion was responsible for the visual disability among members of this family. The lesions found in the maculas of persons of about the same age were almost identical in appearance and the patients' complaints were similar. Consequently, we shall present only two cases, each typical of a phase in the development of the affection.

#### CASE 1

A stenographer (IV, 40; fig. 1) registered at the clinic in June, 1953, complaining of diminished visual acuity in each eye which could not be corrected by lenses. Her vision had been poor as long as she could remember and had become progressively worse during the past 10 years. She had noted an associated difficulty in distinguishing colors. Also, she gave a history suggestive of day blindness in that her visual acuity was better in dim light than in bright light.



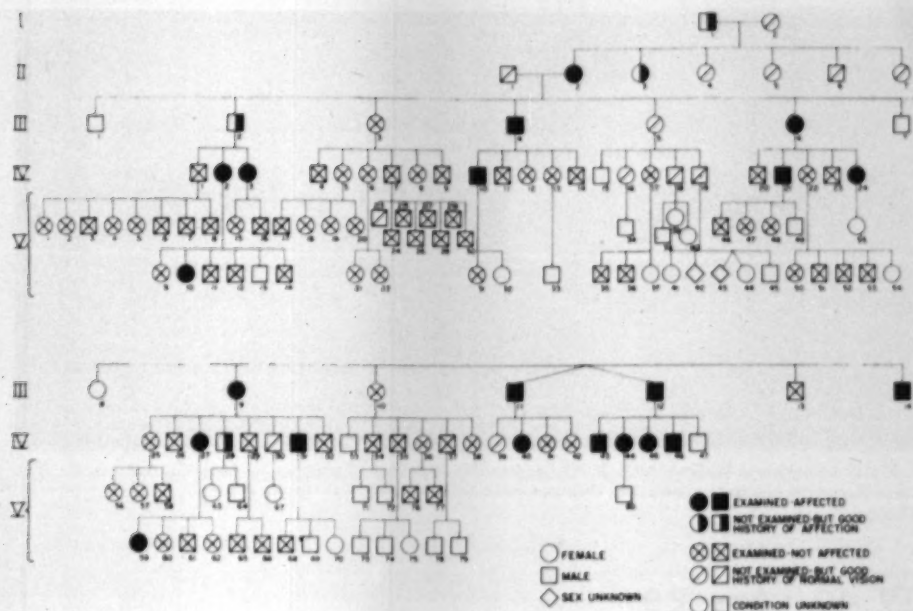


Fig. 1 (Davis and Hollenhorst). Pedigree of family with hereditary macular degeneration transmitted as a dominant trait.

The inquiry revealed that her father and many other relatives had similar or more severe visual involvement.

The examination revealed a healthy, intelligent woman 29 years of age. Visual acuity with correction was: R.E., 6/30, 14/24; L.E., 6/24, 14/24 for distance and near vision, respectively. The results of external ocular examination and examination of the pupils were normal as were ocular rotations and intraocular pressure. Ophthalmoscopic examination showed clear media. A fine, barely perceptible, stippling of pigment was noted in the macula of each eye, with an absence of the foveal reflex. The optic discs were normal (figs. 2a and b).

Examination of the visual fields disclosed normal peripheries, but a very small relative scotoma centrally (fig. 3). Examination with American Optical Company pseudo-isochromatic plates revealed almost complete absence of color sense.

## CASE 2

A 57-year-old white farmer (III, 11; fig. 1) gave a history of progressively poor vision from adolescence until he was about 35 years of age. He thought that his vision had not changed a great deal during the last 15 to 20 years. He gave a history of marked day blindness and color blindness of many years' duration. Because of his day blindness, he preferred to plow at night; he repaired his farm equipment in the darkest corner of his barn.

A record of an examination performed by an ophthalmologist when the patient was 21 years of age revealed 6/15 vision, with correction, in each eye. An examination by an ophthalmologist when the patient was 35 years of age showed a corrected visual acuity of 6/60 in each eye, and complete color blindness.

Our examination revealed the eyes to be normal externally. The corrected visual acuity of each eye was 6/120 and color blind-

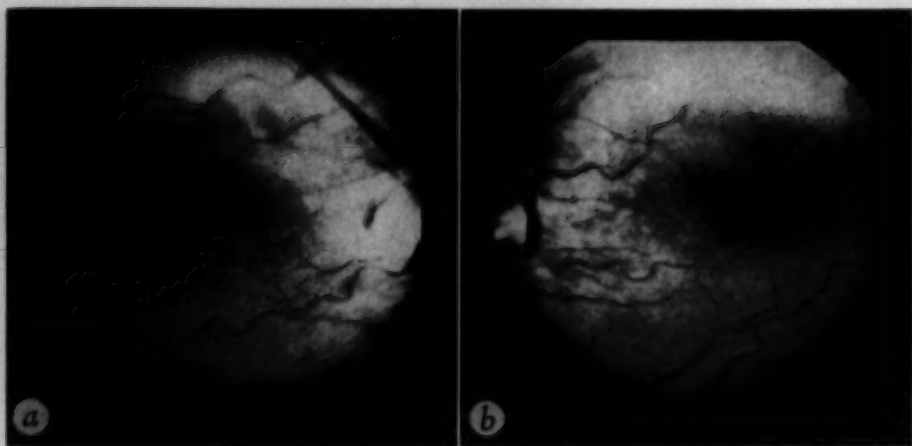


Fig. 2 (Davis and Hollenhorst). Barely perceptible stippling of pigment is shown in each macula. The optic discs are not well shown but their appearance is normal. (a) Right eye (Case 1); (b) left eye (Case 1).

#### IV 40 Age 29

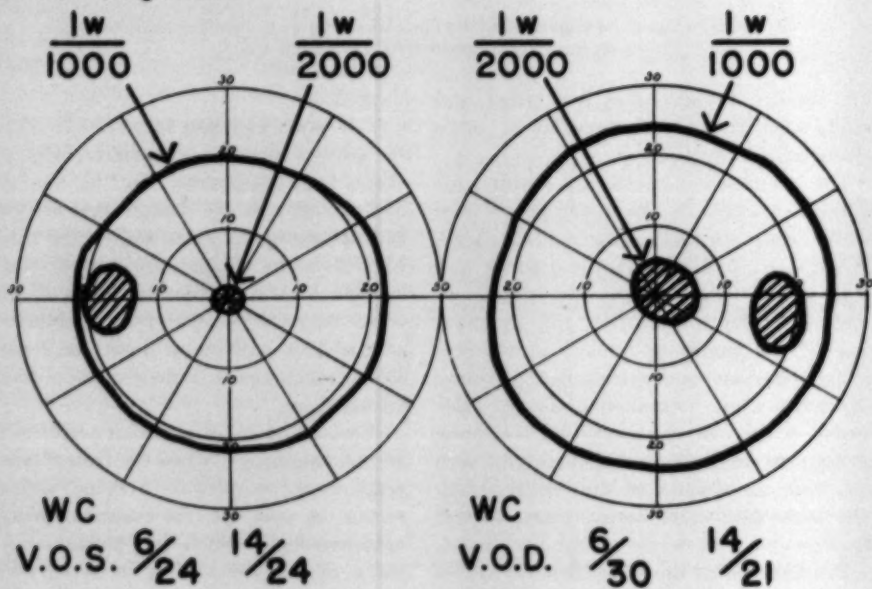


Fig. 3 (Davis and Hollenhorst). Tangent screen fields (Case 1) showing the very relative nature of the scotoma in each eye.

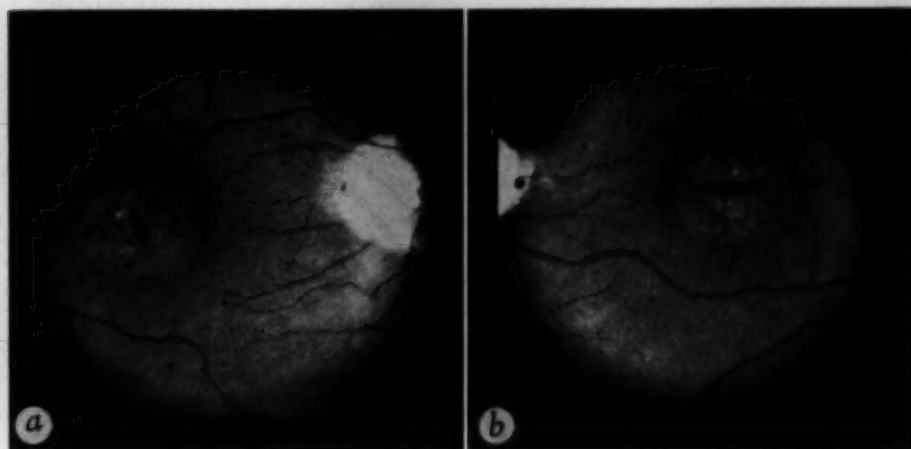


Fig. 4 (Davis and Hollenhorst). Marked pigment disturbance shown in each macula and the mild pallor of the temporal portion of each optic disc. (a) Right eye (Case 2); (b) left eye (Case 2).

ness was complete. Ophthalmoscopy revealed marked pigmentary stippling, approximately 1.5 disc diameters in size, involving the macula of each eye. Mild pallor was noted in the temporal portion of each optic disc (figs. 4a and b). In the visual field of each eye there was a large central scotoma, but the peripheries of the visual fields were normal (fig. 5).

#### COMMENT

A review of the findings in these cases reveals that the course of the disease, the appearance of the lesions ophthalmoscopically, and the other findings in the ocular examination place the disease in the group of heredofamilial degenerations of the macula without cerebral involvement; that is, Sorsby's macular dystrophy. It is difficult to state just where the disease should be placed in Behr's classification based on the patient's age at onset.

Since the onset of symptoms in all of our cases was so gradual the patients found difficulty in giving a history of the exact period when the disease process began. Many of them stated that they had "always had poor vision," but on further questioning we found that the visual defect often was first dis-

covered by the school teacher. Others felt that their vision was fairly good until adolescence or even early adult life.

One of the patients who stated that her vision had been poor all of her life had a history of nystagmus at the age of a few months. Her nystagmus subsequently disappeared. This could indicate involvement at birth or in early infancy. The small number of fifth-generation members known to be affected would tend to indicate an onset at puberty or later.

Though some authors have stated that one of the characteristics of the disease is that all members of one family show the same general age of onset, we feel that this may not necessarily be true for all families and it is not borne out in this study.

All of our patients had bilaterally symmetrical involvement. All affected members in each generation gave essentially the same history of visual impairment, had the same degree of loss of central visual acuity, had essentially similar central scotomas, and showed approximately the same degree of progression of the macular lesions ophthalmoscopically.

The affected patients who could co-operate had rather marked disturbance of color

## III 11, Age 57

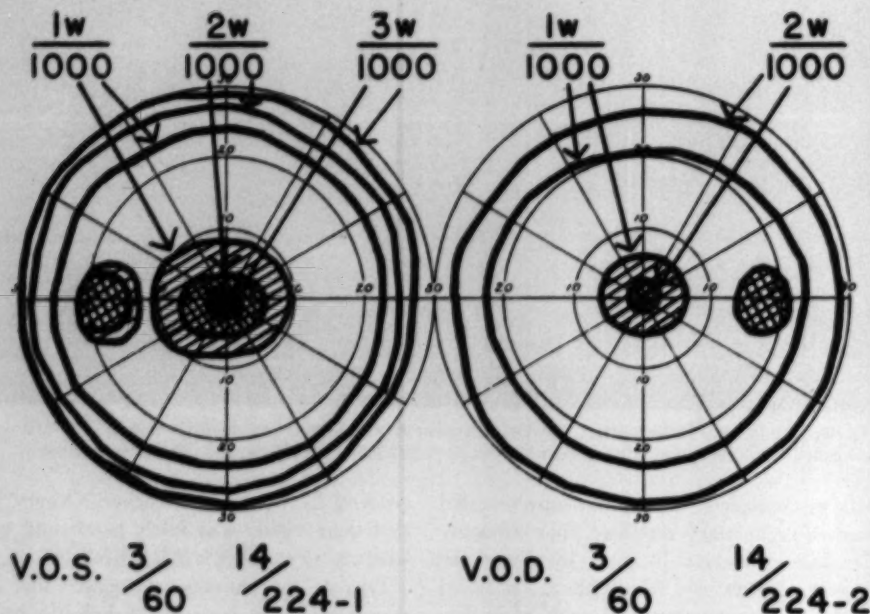


Fig. 5 (Davis and Hollenhorst). Tangent screen fields (Case 2) showing the increased density of the scotomas among the older members of the family.

vision. All who had the disease gave a history suggestive of day blindness. None of the affected or unaffected members of the family showed any evidence of cerebral degeneration, and no member gave a history of involvement of the central nervous system characteristic of cerebromacular degeneration.

The mode of hereditary transmission of this affection is evident when Figure 1 is examined. The macular degeneration is transmitted as a dominant trait with complete penetrance.

#### SUMMARY AND CONCLUSIONS

Degeneration of the macula of each eye occurred in 24 persons in a kinship of 148

members. The age at onset of manifest visual disability varied from very early childhood to adolescence. The lesions were progressive and were symmetrical in each eye. A central scotoma was responsible for the impairment of vision. Marked impairment of color discrimination was associated. Each patient had some degree of day blindness but none had an associated cerebral affection. This defect is transmitted as a dominant trait with complete penetrance. Major mutations were not noted.

*The Mayo Clinic.*

The authors wish to express their appreciation to Dr. George B. McCormick of the Marshfield Clinic, Marshfield, Wisconsin, for his generous co-operation in making available his records for this study.

#### REFERENCES

1. Batten, R. D.: Two brothers with symmetrical disease of the macula, commencing at the age of 14. *Tr. Ophth. Soc. U. Kingdom*, 17:48-49, 1897.

2. Best, F.: Ueber eine hereditäre Maculaafektion: Beitrag zur Vererbungslehre. *Ztschr. f. Augenh.*, **13**:199-212, 1905.
3. Stargardt, K.: Ueber familiäre, progressive Degeneration in der Maculagegend des Auges. *Arch. f. Ophth.*, **71**:534-550 (Sept.) 1909.
4. Behr, C.: Die Heredodegeneration der Makula. *Klin. Monatsbl. f. Augenh.*, **65**:465-505, 1920.
5. Sorsby, A.: The dystrophies of the macula. *Brit. J. Ophth.*, **24**:469-529 (Oct.) 1940.
6. Crawford, J. W.: Familial degeneration of the macula lutea: A review of the literature with a report of eight additional cases. *Am. J. Ophth.*, **25**:525-543 (May) 1942.
7. Falls, H. F.: Hereditary congenital macular degeneration. *Am. J. Human Genet.*, **1**:96-104 (Sept.) 1949.
8. Berkley, W. L., and Bussey, F. R.: Heredodegeneration of the macula. *Am. J. Ophth.*, **32**:361-365 (Mar.) 1949.
9. Mortelmans, L.: Dégénérescence maculaire familiale. *Ophthalmologica*, **120**:157-167, 1950.
10. Klien, B. A.: The heredodegeneration of the macula lutea: Diagnostic and differential diagnostic considerations and a histopathologic report. *Am. J. Ophth.*, **33**:371-379 (Mar.) 1950.
11. Sun, S. F.: Heredodegeneration of the macula lutea: With a report of a case of infantile type without cerebral symptom. *Chinese M. J.*, **69**:440-444 (Sept.-Oct.) 1951.

## CONGENITAL RETINAL FOLD\*

### A CASE REPORT

STEFAN VAN WIEN, M.D., AND WILLIAM B. SULLIVAN, M.D.  
Chicago, Illinois

Ida Mann first recognized the congenital retinal fold as a clinical entity and described it under this name in 1935,<sup>2</sup> although she published a single case in 1928.<sup>1</sup> H. Weve independently published a series of cases of this anomaly as "Ablatio falciformis congenita" in 1936.<sup>3</sup> There have been other reports since. Today, most ophthalmologists are acquainted with this clinical picture that hardly presents diagnostic problems. Few eyes have been excised during the past few years; thus, it seems justified to report the present case which could be examined histologically. The eye was not enucleated because of a mistaken diagnosis but because of uncontrolled glaucoma.

The appearance of a congenital retinal fold is quite characteristic. A septumlike veil extends from the optic disc toward the extreme periphery and attaches to the region of the ora serrata as well as, in most instances, to the equator of the lens. The crest

of the fold usually has an elevation of approximately 10 diopters.

It seems that the majority of cases reported were situated in the inferior temporal quadrant, although other locations have been described. In a number of instances, the folds were bilateral and, in these cases, symmetrical. One or more vessels originating from the trunk of the central retinal vessels run along the crest of the fold; as a rule whether they are arteries or veins cannot be decided from the ophthalmoscopic appearance. A number of folds reported occurred in several members of the same family.

### CASE REPORT

R. D., a well-developed, well-nourished, white female infant, was seen originally by one of us (W. B. S.) at the age of six months in June, 1948. The presenting complaint was failure of the baby to follow light. Except for this observation, the patient appeared healthy and normal in all respects. The past history revealed premature birth at six and one-half months, and a birth weight of two pounds, three ounces. Mater-

\*From the Department of Ophthalmology, Northwestern University Medical School. Presented before the Chicago Ophthalmological Society, May 17, 1954.



nal health was good during the pregnancy, and the delivery was spontaneous and uncomplicated. No illness of significance occurred in the infant's first six months; growth and development were normal.

*Eye findings.* Office examination revealed an essentially normal left eye. Marked right exotropia and right microphthalmos were noted. The right anterior chamber was shallow; the pupil was sluggish to light and measured 2.5 mm. as compared to a normal left pupil of 3.5 mm. Office fundus study was unsatisfactory.

Examination under general anesthesia revealed a Schiøtz tension of 15 mm. Hg in each eye. Transillumination was normal. The left fundus was myopic but otherwise normal. In the right eye there was a web-like remnant of the tunica vasculosa lentis on the anterior lens surface. Numerous floaters were present in a fluid vitreous. A vague grayish strandlike elevation of retina arose at the nasal edge of the disc. It ran forward into the vitreous and temporally to the region of the ora serrata, where it merged into a domelike whitish elevation of retina.

The possibility of an arrested retrolental fibroplasia was considered, and further observation was advised.

The child did not reappear for examination for two years. By this time she had been established as a case of cerebral palsy, on

management for about one year. Office examination added nothing to previously recorded findings and examination under general anesthesia was declined. X-ray examination of the skull at that time was negative.

Only sporadic follow-up was possible in the next four years. During this interval a marked emotional instability and moderate mental retardation were noted.

The right eye underwent several attacks of iridocyclitis which eventually caused an anterior peripheral synechia of the iris in the 4- to 5-o'clock position. Ultimately a secondary glaucoma ensued, with a Schiøtz tension measuring between 68 to 70 mm. Hg. A clinical diagnosis of pseudoglioma, falciform fold, and secondary glaucoma was made. The eye was enucleated in June, 1953.

The specimen was opened by two horizontal calottes, the lower one entering the anterior chamber. An anterior peripheral synechia was seen in the nasal chamber angle. A grayish fold extended from the disc to the temporal equator of the lens.

#### HISTOLOGIC FINDINGS

The corneal epithelium, Bowman's membrane, and the corneal stroma are intact. There is no evidence of trauma. In some sections (fig. 1), the anterior surface of the iris is adherent to the posterior surface of the cornea, thus obliterating the nasal cham-

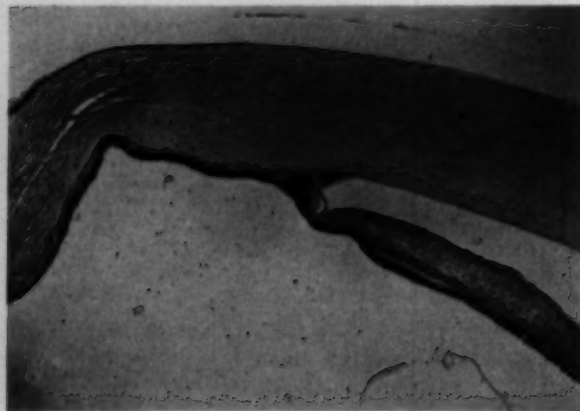
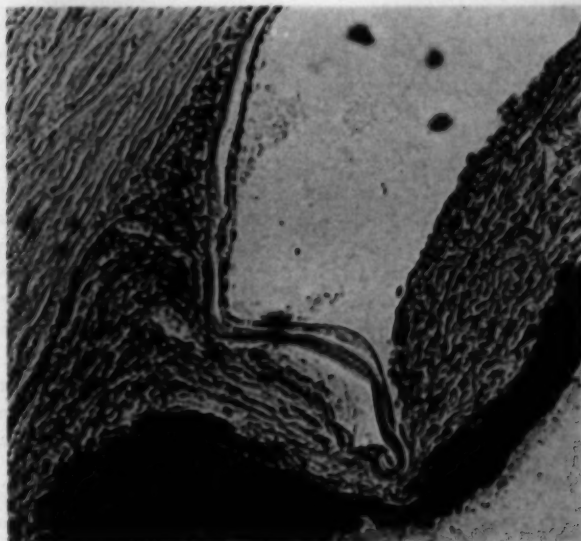


Fig. 1 (Van Wien and Sullivan). Nasal chamber angle. Extensive peripheral synechia with atrophy of iris stroma; intercalary staphyloma.

Fig. 2 (Van Wien and Sullivan). High-power view of Figure 1. Descemet's membrane extends over a pseudo-angle to the iris where it ends abruptly.



ber angle for a distance of about three mm. The iris stroma in the area of this anterior peripheral synchia is quite atrophic.

Descemet's membrane and the corneal endothelium cannot be identified. However, Descemet's membrane reflects over the pseudo-angle to the iris where it ends abruptly (fig. 2). The trabecular meshwork partly covers the temporal chamber angle (fig. 3).

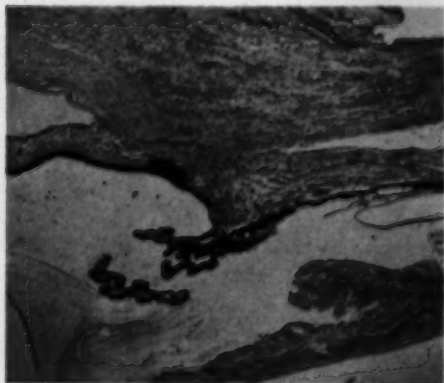


Fig. 3 (Van Wien and Sullivan). Temporal chamber angle. Trabecular meshwork covers chamber angle; retina fold is not attached to atrophic ciliary processes.

No inflammatory cells are seen in the iris; in fact, there is no evidence of inflammation anywhere. There is a beginning intercalary staphyloma at the nasal side. Schlemm's canal cannot be recognized with certainty in any section. The ciliary processes are quite atrophic.

A retinal fold originates from the disc and involves the entire temporal half of the retina (fig. 4). This fold does not include the pigment layer. It does consist of very poorly differentiated retinal elements and proliferated glial tissue, although some connective-tissue strands can be demonstrated with van Gieson stain.

The fold attaches itself firmly to the ora serrata (fig. 5), as well as to the posterior equatorial region of the lens, the latter attachment being caused by a connective tissue plate. There are no adhesions between the fold and the ciliary processes (fig. 3). Numerous rosettes are noted in the fold, especially anteriorly.

Slightly behind the ora serrata, there is a very flat retinal detachment. In this area, there are quite a number of bizarre secondary drusen.

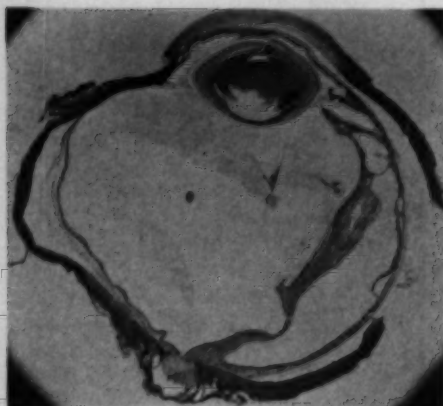


Fig. 4 (Van Wien and Sullivan). Congenital fold originating from optic disc and extending temporally to ora serrata and equator of lens.

The nasal half of the retina is poorly developed. Rods and cones are missing in many places. The nuclear layers are partly fused. The population of the ganglion-cell layer is reduced or completely absent. The nerve-fiber layer shows microcystic degeneration.

#### COMMENT

For the purpose of this report, we need not review in detail the literature on the subject. Ida Mann's<sup>2</sup> explanation for the developmental mechanism of the fold is generally accepted today.

According to her, the primary vitreous becomes attached in one area to the inner layer of the optic cup. The secondary vitreous which separates these two structures fails to do so in the area where the adhesion has formed. Therefore, the inner cup in this region is prevented from coaptation with the outer layer but is raised in the form of a ridge.

Mann was able to find a hyaloid vessel on the surface of the fold in every case—even if it was evidenced by only a few strands. Such a hyaloid vessel is considered essential in causing the previously mentioned adhesion. Other investigators have failed to mention the absence or presence of a hyaloid vessel attached to the retinal fold. Only Til-

lema<sup>4</sup> mentioned specifically that he was unable to demonstrate a hyaloid vessel. Since his case showed evidence of a previous inflammation, he concluded that there must be cases of this nature which are not developmental anomalies but results of inflammation.

Weve<sup>5</sup> assumes that there is a connective-tissue adhesion between the equator of the lens and the ora serrata. Shrinkage of this connective-tissue band or growth of the globe causes a tentlike detachment of the retina.

Kiewe<sup>6</sup> interprets the slight protrusion of the disc over the level of the retina in his case and that of Ancona as due to the persistence of von Szily's "Schaltstueck" (the intercalated neuron), which is the anlage for the primitive papilla of the optic nerve.

Van Manen<sup>6</sup> actually found a persistent Bergmeister papilla in his case of congenital retinal fold. This may support Kiewe's view, which otherwise is not generally accepted.

None of these explanations really accounts for three characteristics of the congenital fold: (1) Its predilection for the inferior temporal quadrant, (2) its bilateral occur-



Fig. 5 (Van Wien and Sullivan). Retinal fold is firmly attached to ora serrata.

rence, and (3) its definitely hereditary trend.

Undoubtedly, there are cases without hyaloid vessels attached to the fold (including the case presented here). This would suggest that Ida Mann's explanation is not true for all cases. A number of reports either fail to mention an adhesion of the fold to the equator of the lens, or specifically stress its absence. Weve's explanation, of course, is based on the existence of such an adhesion.

Finally, the three cases of Ancona, Kiewe, and Van Manen are isolated instances of either a persistent Schaltstueck or Bergmeister papilla and, therefore, lack the basis for a mechanism that could be considered true for the majority of cases of congenital retinal folds.

It is quite possible that we are not dealing with a clinical entity but with a number of different processes, all of which could result in retinal folds. Some of them, examined ophthalmoscopically only, may well have been the end-result of arrested retrolental fibroplasia. In "A classification of retrolental fibroplasia," adopted by the National Society for the Prevention of Blindness,<sup>7</sup> one illustration, could easily be mistaken for a typical congenital fold.

On the other hand, Terry based his original paper, "Fibroplastic overgrowth of persistent tunica vasculosa lentis in premature infants," on seven cases. Two years later, he excluded one case when the same manifestations occurred in another member of the same family (see Krause<sup>8</sup>). Histologic examination of that eye, interestingly enough, failed to reveal a hyaloid vessel. A large mass of glial tissue extended from the

optic nerve to attach itself to the ora serrata and the lens.

Teng and Katzin<sup>9</sup> described congenital folds at the ora serrata in one of their cases. This type of fold seems entirely unrelated to the one under discussion.

Krause,<sup>8</sup> in his original report on encephalo-ophthalmic dysplasia, included one case (the 17th) with congenital bilateral folds. He observed that patient only clinically. The intraocular pressure in this 20-month-old infant was: R.E., 10 mm. Hg; L.E. 16 mm. Hg (Schiötz). It is interesting to note that, in that series of 16 enucleated eyes, 12 showed an undeveloped filtration angle or anomalous Schlemm's canal. Ten of these eyes had increased pressure; no glaucoma was present in any eye with a normally functioning chamber angle.

The patient presented in this report had a normal left eye; whereas, all of Krause's cases had bilateral involvement. The glaucoma, of course, could be a result of the extensive peripheral anterior synechia. Yet, in the absence of any inflammation, it might well be possible that the iridocyclitic episodes mentioned in the history actually were glaucomatous attacks, and that the occlusion of the chamber angle was not the cause but the result of glaucoma.

One is not justified in drawing conclusions on the basis of an isolated case. Yet, if one admits the possibility that congenital retinal folds might be the result of various etiologic factors, encephalo-ophthalmic dysplasia could well be one of them.

104 South Michigan Avenue (3).

8000 South Racine Avenue.

#### REFERENCES

1. Mann, I.: A case of congenital abnormality of the retina. *Tr. Ophth. Soc. U. Kingdom*, **48**:383, 1928.
2. ———: Congenital retinal fold. *Brit. J. Ophth.*, **19**:641, 1935.
3. Weve, H.: Ueber "Ablatio falciformis congenita." *Arch. f. Augenh.*, **109**:371, 1936.
4. Tillema, A.: Infantile and congenital retinal fold. *Brit. J. Ophth.*, **21**:94, 1937.
5. Kiewe, P.: Beitrag zur Kenntnis der angeborenen Missbildungen des menschlichen Auges. *Arch. f. Ophth.*, **135**:220, 1936.
6. Van Manen, J. G.: Congenital anomaly of the fundus. *Arch. Ophth.*, **26**:1, 1941.
7. A classification of retrolental fibroplasia. *Am. J. Ophth.*, **36**:1333, 1953.
8. Krause, A. C.: Congenital encephalo-ophthalmic dysplasia. *Arch. Ophth.*, **36**:387, 1946.
9. Teng, C. C., and Katzin, H. M.: An anatomic study of the peripheral retina. *Am. J. Ophth.*, **36**:169, 1953.

## MACULAR HOLES IN RETINAL SEPARATIONS\*

### THEIR SIGNIFICANCE AND THEIR SURGERY

ARTHUR H. KEENEY, M.D.

Louisville, Kentucky

The recent studies of Della Porta<sup>1</sup> on transbulbar endodiatrhermy for lesions which appear to be macular holes associated with retinal separations focus attention on the fundamental relationship of such lesions to retinal separations.

The purpose of this paper is to analyze the triphasic role of macular holes in retinal separations and to discuss factors involved in their surgical repair.

Macular holes were recognized (J. H. Knapp, 1869) shortly after the ophthalmoscope was invented or nearly 100 years ago. Their usual causation and pathology, however, were not appreciated until the turn of the century (Collins, 1900; Haab, 1900; Ogilvie, 1900; Kuhnt, 1900). Particular inquiry into their relation to retinal separation has a history of only about 15 years.

Macular holes are generally due to (1) contusion or (2) degenerative changes associated with vascular or inflammatory pathologic processes. In any case there is first a formation of cystic spaces due to edema, particularly in the layer of Henle. Multiple small cysts or a few large cysts may thus develop and, by coalescence, form the typical dark-red circular spot with a punched-out appearance at the fovea.

It is particularly significant that simple macular holes of the common degenerative type never produce true retinal separation. At most, they rarely lead to a localized shallow retinal elevation in the perimacular area. Normal retinal position may be maintained in the presence of punched-out macular lesions by three possible mechanisms:

*First*, many of these apparent holes are

actually cysts with an intact, internal limiting membrane covering their inner wall and maintaining retinal continuity. This may be demonstrated histologically<sup>2</sup> but the internal limiting membrane or inner cyst wall is often too thin to survive tissue preparation. Clinically, however, the inner cyst wall may be visualized by the reflex seen on its surface in careful ophthalmoscopy or by slit illumination of the area.

*Second*, such a macular cyst may rupture through its inner wall only, leaving an intact external wall which maintains retinal continuity. As these cysts extend through the outer nuclear layer, their walls may unite with the external limiting membrane. Usually this is seen with ease in histologic sections, but it is most difficult to establish with the ophthalmoscope.

*Third*, the formation of cystic degenerative changes may cause mild, localized inflammation with subsequent adhesions in the perimacular area. This is actually the sealing of a retinal break by natural processes.

In the first two situations, the macular holes are actually incomplete; in the third, they may extend completely or incompletely through the retina; when complete, they may show a localized and shallow retinal elevation.

Apparent macular holes may be associated in three ways with retinal separations involving the posterior pole:

A. When extending completely through the retina, they may very rarely be the antecedent, causative pathologic condition. In such cases, the separation usually does not involve the retinal periphery.

B. When incomplete, these holes may be the incidental, associated pathologic alteration. Of no significance in planning surgery,

\*From the University of Louisville School of Medicine, Section on Ophthalmology. Presented at the VII Annual Clinical Conference of the Wills Eye Hospital, Philadelphia, February 18, 1955.



they make the prognosis, especially in regard to central vision, poor. Such a lesion does not influence the prognosis for reapposition of the retina and is more likely to be found in severe contusion cases.

C. The hole may be a secondary or subsequent alteration found in long-standing separations, particularly those of the idiopathic type.

#### PLANNING SURGERY

In planning the surgery of retinal separations which include the macula and in which there are apparent macular holes, it is important to establish whether the hole is complete or incomplete and to evaluate its time-cause relation to the separation. If such a dark-red circular lesion be operculated, one is fairly certain that the hole is complete and will have to be sealed. If an inner cyst wall can be demonstrated by the light reflex on its convexity or by slit-ophthalmoscopy, the hole is incomplete and should be omitted from surgical attack. In these cases there are usually definite holes in the periphery which must, of course, be given a watertight seal by surgery.

The differentiation between complete and incomplete macular breaks is difficult but the cystic lesions—in contradistinction to the complete holes—often present slightly irregular outlines and smaller adjacent cysts. These are best seen in red-free and adjacent (proximal) illumination.

The cardinal principle in retinopexy is to seal each break completely but with minimum trauma. If there is any uncertainty about a macular hole being complete, it is prudent and statistically wiser to omit it from surgical attack. If the separation also involves the periphery and peripheral breaks can be detected, it is practically certain that an associated macular hole is incomplete and should be avoided at surgery. The surgical sealing of complete macular breaks requires particular caution to conserve maximum perimacular acuity. Figure 1, based on studies by Ludvigh,<sup>3</sup> graphically illustrates average visual-acuity values in the macular region.

Diathermy with penetrating electrodes (large and small Walker micropins; Safar nails, 1.5 to 2.5 mm. long; Gradle conical needle, 1.5 by 0.5 mm.; larger Liebel-Flar-

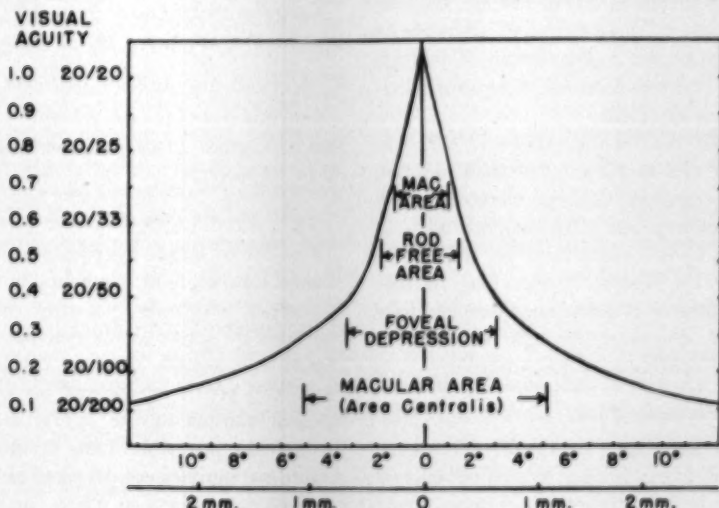


Fig. 1 (Keeney). Average relations of macular details.  
(Based on studies by Ludvigh.<sup>3</sup>)

sheim electrodes; Meesmann perforating needle; and so forth) must not be used because they produce relatively wide areas of destruction. Thus a one-mm. macular hole might give the prognosis of a potential acuity of 20/60 to 20/80 but, if rimmed with penetrating coagulation, maximum acuity could easily drop to 20/200 or less.

The destructive action of diathermy generally involves an area about twice the diameter of the grayish retinal reaction seen ophthalmoscopically. Thus a watertight seal can be made by diathermy with apparently uncoagulated spaces between each point of application which are equal in diameter to the areas of heat reaction.

#### AGENTS FOR SEALING HOLES

Possible agents for sealing macular holes are:

#### 1. DIATHERMY

Current sources are: Walker high frequency unit; Cameron; Castroviejo; Keeler; Ophthalmotherm of Sanitas; Thermo-flux of Siemens; Walter; Arruga.

a. *Surface*. Weve (1930): three to four-mm. ball electrode at 100 to 150 ma. Larssen (1930): two to three-mm. ball electrode at 40 ma. Castroviejo angular electrode. Arruga angulated surface electrode. Schepens transilluminating electrode.

b. *Partial penetrating*. Weve (1932): 30 to 40 ma. (75 to 80°C.). Pischel, Guyton, Kronfeld angulated 0.5-mm. electrodes with current delivery less than one second.

c. *Transbulbar endodiathermy of Dellaporta* (1951). Needle 30-mm. long by 0.5-mm. in diameter is introduced through pars plana and followed through vitreous to macula by ophthalmoscopic control.

#### 2. ELECTROLYSIS

a. *Cathodal*. Vogt (1934): 0.1-mm. diameter needle, 1.0 to 1.5 ma. Watch bubbles of hydrogen; least damaging of all procedures; controlled by direct ophthalmoscopic observation.

b. *Anodal*. Imre (1932).

c. *Bipolar*. von Szily and Machemer (1934): (1) Surface—tips 1.0-mm. apart, 30 ma. for up to 10 seconds; (2) penetrating—up to 200 ma. for five seconds.

#### 3. CHEMICAL CAUTERIZATION

Chemical cauterization is done through scleral trephine openings one-mm. in diameter.

a. *KOH* (two to six percent). Quist, Lindner (Unterminierungsmethode, 1933): inject 0.01 to 0.02 cc. and neutralize with 0.5 to 10-percent acetic acid; may use KOH pencil of Guist. These procedures are more destructive than electrolysis.

b. *NaOH* stick. Arruga (1932).

c. *Other chemicals*. Tincture of iodine (Schoeler, 1899; Deutschmann, 1933). Carbolic acid, chromium dioxide, and so forth.

#### 4. CRYOCAUTERY

Carbon-dioxide snow was used by Deutschmann (1933). Steam jets have also been tried as an opposite technique, Jensen (1904).

#### 5. THERMOPHORE

Langdon (1935) used 71 to 74°C. for one minute. An angulated tip is used.

#### 6. SCLERAL DIATHERMOCOAGULATOR

For this technique the 2.5-mm. pyrometric ball of Coppez (1930) is used at 80°C. for 20 to 30 seconds.

#### DISCUSSION

The use of larger instruments such as the Shahan thermophore, trephines, or even the Lacarrere electrode presents mechanical problems of access to the macula. Adequate exposure is usually obtained by division of the lateral rectus muscle and use of 4-0 silk traction sutures at the lateral limbus and through the insertion of the divided muscle. Additional muscles are detached only if indicated to gain access to other (nonmacular) portions of the separation. Guist originally used a Krönlein type of orbitotomy to

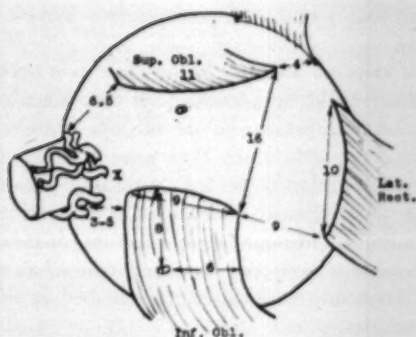


Fig. 2 (Keeney). Approximate and average relations of the structures about the macula. (After Fink, W. H.\*)

approach macular holes, but this is not necessary.

Figure 2 illustrates the average anatomic relations about the macula but variations of one to three mm. commonly occur in all these structures. The posterior edge of the insertion of the inferior oblique muscle is a fairly reliable guide to the site of the macula which is generally two to three mm. obliquely above and proximal to that point. Vortex veins and the optic nerve must always be avoided.

Of the available techniques, the high frequency diathermy source such as the Walker or Ophthalmotherm units with partial penetrating electrodes are most convenient. The angled 0.5-mm. pins of Pischel, Guyton, or Kronfeld are effective and easily directed about the macula. Engagement of these short pins in the sclera obviates sliding, slipping, and possible dissipation of current which may occur with surface electrodes. The double-pronged Berens hook is at times helpful in maintaining good exposure of the macular area. Current should be kept low enough to produce only a faintly perceptible, greenish-tinged, scleral discoloration at the immediate site of application.

#### REPORT OF CASES

The following cases illustrate the two most common types of macular holes associated

with retinal separations which include the macular area.

#### CASE 1

A 20-year-old white man was first seen on October 17, 1952, complaining of painless impairment of vision in the right eye since it was struck by a flying nail on March 6, 1952.

Examination of the left eye and right anterior segment was negative. Vision, O.D., was 1/200 with accurate light projection. The vitreous of the right eye was semifluid and contained a few small opacities. The retina was separated and elevated in all quadrants except the superior-nasal.

A typical, large, dark-red, punched-out hole was seen in the detached macula and no anterior cyst wall could be demonstrated. A large oval hole was present in the 8-o'clock periphery, and shallow retinal folds radiated above and below the macula toward the 7- and 10-o'clock positions.

On bedrest and binocular dressings in the hospital there was good settling after three days. The large peripheral hole was sealed with 12 Walker micropins and a moderate amount of thick inter-retinal fluid was released on extraction of these pins. Surface coagulation with the 0.5-mm. Pischel pin was done temporally and inferiorly. Binocular dressings were maintained for three weeks and then three-mm. pinhole goggles were substituted. Activity was then slowly resumed.

The entire retina and macular area were well reattached. Vision has improved from 1/200 to 20/150 and the peripheral field has continued full for nearly two years of post-operative observation.

*Comment.* Because of the large coexisting peripheral break in this case, it was felt that the macular lesion was not a complete hole, but rather a postcontusion cyst which had ruptured through its inner wall only. On these grounds no surgery was directed to the macular area.

The visual improvement and complete re-

attachment give final proof that the macular hole was incomplete. Such a result could not have been achieved without diathermy to the macula if the hole had been complete.

#### CASE 2

This case is reported through the courtesy of Dr. Kurt Ackerman.

An 11-year-old white boy was first seen on March 2, 1954, complaining of painless impairment of vision in the right eye since a contusion injury sustained two years earlier.

Examination of the left eye and the right anterior segment was negative. Vision, O.D., was 2/200 with accurate light projection. Scattered, small opacities were present in the vitreous of the right eye. The retina was separated throughout both temporal quadrants and the macular area. The maximum elevation was in the inferior temporal quadrant. Small disinsertions were present at the 8- and 10-o'clock positions.

A dark-red, holelike lesion was present in the detached macula. On minute inspection, the border of this lesion appeared somewhat irregular, rather than perfectly circular, and five small, clear cysts could be identified within the apparent hole by virtue of the light reflexes on their convex and intact inner surfaces.

On bedrest and binocular dressings in the hospital, there was good settling within a few days. At retinopexy, a double-row of Walker micropins was placed about each of the disinsertions and extended to the ora serrata. A fair amount of inter-retinal fluid was released on extraction of the pins. Postoperative management was similar to that in the first case.

The entire retina and macular area were well reattached and vision improved from 2/200 to 20/400. This has been maintained

for four months of postoperative observation.

*Comment.* Because of the inner cyst walls which could be identified in this macular lesion, and because of the obvious disinsertions, the indications here were twofold to avoid the macula during retinopexy. Again the final, clinical evidence of actual retinal continuity through a punched-out macular lesion has been the sustained reattachment without any surgical efforts directed to the posterior pole.

#### SUMMARY

Macular holes are due to contusion or degeneration but in either event cystic degenerative changes precede the typical hole formation. Simple, degenerative holes do not lead to retinal separation. Proper retinal position is maintained in the presence of typical, punched-out lesions when:

1. The hole is actually a cyst with an intact inner wall, as in Case 2.
2. Such a macular cyst has ruptured through its inner wall only, thus leaving an intact outer wall, as in Case 1.
3. Perimacular adhesions between the choroid and retina have been created by local inflammation.

Macular holes are rarely the cause of retinal separation, in which case they must be complete holes. More commonly they are incomplete and incidental to the pathogenesis of separation, as in the two cases presented. Subsequent alterations—complete or incomplete—may be found in separations of long standing.

When macular holes are incomplete they should *not* be subjected to surgery with its attendant loss of valuable perimacular acuity. Sealing of complete macular breaks should be done with small, partial-penetrating electrodes using low current, directed precisely to the edges of the hole.

1103 Heyburn Building (2).

#### REFERENCES

1. Dellaporta, A.: Endodiathermy: A method for sealing macular holes by transbulbar coagulation. *Am. J. Ophth.*, 37:649-656 (May) 1954.



2. Kornzweig, A. L., and Feldstein, M.: Hole in the macula: A clinico-pathologic study. *Am. J. Ophthalm.*, **33**:243, 1950.
3. Ludvigh, E.: Extrafoveal visual acuity as measured by Snellen test letters. *Am. J. Ophthalm.*, **24**:303, 1941.
4. Fink, W. H.: Anatomy of the extrinsic muscles of the eye. *Strabismus Ophthalmic Symposium*. St. Louis, Mosby, 1950.

## EFFECTIVE TREATMENT OF TUBERCULOUS CHOROIDITIS\*

JAMES E. LEBENSOHN, M.D.

*Chicago, Illinois*

The first attempt to cure tuberculosis by chemotherapy was made by Robert Koch with the salts of gold in 1890. The disillusionment which followed was the fate of all successive remedies until the advent of streptomycin in 1945. The second advance came in 1946 when J. Lehmann of Sweden discovered that the simultaneous administration of *p*-aminosalicylic acid helped to overcome bacilli resistant to streptomycin. A recent and powerful ally in the chemico-antibiotic attack on tuberculosis is the hydrazine derivative of isonicotinic acid, now known as isoniazid, which was introduced by American investigators in the early part of 1952. This agent inhibits the growth of both streptomycin-sensitive and streptomycin-resistant bacilli in a dilution of 1 to 60 million in vitro. Its activity is unusually specific; only the *Mycobacterium tuberculosis* is affected, and it exhibits almost no potency against other germs, pathogenic or nonpathogenic. Isoniazid is nontoxic in therapeutic dosage, is rapidly absorbed, speedily penetrates all tissues and fluids, and is as active against the tubercle bacilli in vivo as it is in vitro. Several investigators have demonstrated that isoniazid can effect a definite cure in experimentally induced ocular tuberculosis—a result never achieved before.

A detailed study was communicated as early as June 27, 1952, by Lepri, Capalbi, and del Vivo.<sup>1</sup> In 52 rabbits the anterior chamber was inoculated with human tubercle

bacilli. The nontreated controls showed ocular inflammation at about the eighth day, iridic tubercles by the 10th day, then corneal vascularization and pannus, and finally after 30 to 45 days buphthalmos with or without perforation. In rabbits given isoniazid from the day following inoculation no ocular inflammation ensued. In one subgroup, in which isoniazid was stopped after 25 days, ocular inflammation appeared three weeks later in attenuated form but with the subsequent evolution of tubercles in the cornea and iris. In the second subgroups in which isoniazid was discontinued after 45 days of continuous treatment, a mild ocular inflammation of short duration appeared five weeks later; but in the third subgroup in which isoniazid was administered for 65 days, no inflammatory episode whatsoever followed the cessation of treatment. Isoniazid therapy was instituted in a fourth subgroup 15 days after inoculation when the tubercular reaction in the eye was well marked with the result that the inflammatory symptoms rapidly regressed to clinical resolution in five weeks. Treatment was consistently more effective when streptomycin was added to the isoniazid regimen and was further enhanced when *p*-aminosalicylic acid was included also.

The infectivity of eyes at various stages of treatment was tested by injecting a suspension of uveal tissue in the peritoneum of guinea pigs and into the anterior chamber of normal rabbits. The test was negative always when the inoculated rabbits had been treated continuously with isoniazid for 60 days; or with isoniazid, streptomycin, and *p*-amino-

\*From the Department of Ophthalmology, Northwestern University Medical School. Read before the Chicago Ophthalmological Society, January 18, 1954.



salicylic acid for 40 days. The cutaneous response to tuberculin, tested five weeks after inoculation, was positive to the same degree in both the untreated rabbits with florid ocular tuberculosis and the animals under continuous treatment who had never shown an inflammatory response. The focal reaction to tuberculin, however, was marked in the former group and absent in the latter.

Similar results in the control of experimental ocular tuberculosis have been reported by Goulding and Robson,<sup>2</sup> Pannarale and Leonardi,<sup>3</sup> Knapp and von Sallmann,<sup>4</sup> Kratka and Leopold,<sup>5</sup> Bruna<sup>6</sup> observed that, when ocular tuberculosis reappeared after insufficient treatment, the recurrences were frequently not benefited by resumption of isoniazid medication, probably due to a drug resistance acquired by the bacilli. He noted that the isoniazid in the aqueous after intramuscular injection attained a concentration of one third of that in the plasma.<sup>7</sup>

Simonelli and Rizzini<sup>8</sup> found that in both rabbit and man a solution of isoniazid was well tolerated when instilled in the eye or injected subconjunctivally. In the rabbit a subconjunctival injection of 50 mg. was followed by a concentration in the aqueous up to 140 gamma or nearly three times that attained when the same amount was injected intramuscularly.

Alagna<sup>9</sup> demonstrated that the instillation of an isoniazid solution penetrated the aqueous and rapidly reached a therapeutic level. In the experimentally produced corneal lesions of tuberculosis in the rabbit, isoniazid hastened the disappearance of corneal vascularization and opacities.

The clinical results of isoniazid therapy so far recorded have been most heartening. Eli Bard<sup>10</sup> presented before the Colorado Ophthalmological Society on October 31, 1952, a 19-year-old woman with bilateral tuberculous choroiditis who had been treated previously with streptomycin and *p*-aminosalicylic acid without help. In July, 1952, vision was limited to light perception in each eye and a serous detachment had developed in

the right eye. After two weeks of isoniazid therapy the acuity of the right eye was 20/20-3. Dolcet<sup>11</sup> in examining children with tuberculous meningitis under isoniazid therapy, noted healing of the choroidal tubercles and absorption of associated papillary edema. Schlaegel and Hungerford<sup>12</sup> used isoniazid in human cases of granulomatous uveitis and found that the degree of favorable response followed the likelihood of tuberculous etiology. Borioni<sup>13</sup> also reported good results with isoniazid in severe cases of ocular tuberculosis in adults.

#### TUBERCULIN

Tuberculin has had a certain vogue in the treatment of ocular tuberculosis, mainly because of the lack until recently of a more rational alternative. Even so, many considered tuberculin therapy as discredited. The late Alfred Vogt stated in 1941 in the third volume of his *Slit-lamp Microscopy of the Living Eye*: "As regards the specific therapy of tuberculosis, practical experience had resulted in its more or less unanimous rejection, and it has been borne in upon the ophthalmological world at large that this specific treatment involves such dangers that it must, in a general way, be abandoned. Thus most ophthalmologists have given up tuberculin and allied methods and have gone back to physical therapy and treatment by diet."

About 20 years ago an architect, aged 35 years, visited me because of a recent attack of tuberculous-choroiditis in one eye. After receiving my opinion, he consulted Dr. Harry Gradle who treated him with tuberculin. When I saw the patient three years later the eye had become blind, atrophic and painful, and required enucleation. Dr. Gradle always stressed thereafter the danger of tuberculin for disease of the posterior segment. The literature is replete with similar cases including reports in recent years. In 1950, Onfray and Onfray<sup>14</sup> recorded a disastrous focal reaction to purified tuberculin which necessitated enucleation, and Peric-

Sajveit<sup>15</sup> saw a case of tuberculosis of the choroid with retinal detachment which resulted from a focal reaction to tuberculin therapy.

#### CASE REPORTS

##### CASE 1

An executive, aged 48 years, of robust appearance and weighing 185 pounds, was referred to me July 16, 1953, because of a rapid loss of vision in the left eye. He had noted purple spots before this eye during the previous week and in the past four days had experienced a sensation of pain in the area of the left upper lid and brow. The oculist who had refracted him four years before wrote that his unaided acuity was then R.E., 20/15; L.E., 20/15, and that his distance correction was then plano for each eye.

At the present examination the acuity was 20/20 for the right eye, but with the left eye he could see only the end digits of my outstretched fingers. The left eyeball was sensitive to touch in the ciliary region.

The ophthalmoscope revealed in the right eye numerous yellowish and partly pigmented spots scattered through the entire fundus in the vicinity of the blood vessels and some exudative strands in the posterior vitreous. The left eye had a light, powdery opacity of the vitreous, a similar fundus picture, and also an elevation in the macular area of about four diopters surmounted by small striate hemorrhages and surrounded by retinal edema.

The intraocular pressure of each eye was normal.

The left eye was treated with atropine because of the associated cyclitis and the patient was hospitalized for further study. The Vollmer patch test, repeated twice, was four-plus. X-ray studies of the lungs showed a Ghon complex but no present active pathologic condition.

The red blood cell count was 4.1 million; the white cell count 6,350: eosinophiles 2, polymorphonuclears 57, lymphocytes 40, monocytes 1. The hemoglobin was 84 per-

cent; blood sugar, 90 mg.; urea, 40 mg. The blood pressure was 125/80 mm. Hg. A heart murmur was noted.

The following test, described by Kapus-cinki,<sup>16</sup> added further evidence to the diagnosis of tuberculous choroiditis. Intravenous injection of typhoid vaccine increased the reaction of the cutaneous tuberculin test and caused a mild but definite focal reaction.

On July 24th, the simplified chemo-antibiotic regimen currently used in the treatment of pulmonary tuberculosis<sup>17</sup> was started and continued for six months. The patient took orally isoniazid (150 mg. morning and night) and *p*-aminosalicylic acid (seven 0.5 gm. tablets after each meal). Twice weekly streptomycin was injected in the gluteal muscles (one gm. dissolved in four cc. isotonic saline).

By July 28th, the cyclitic symptoms were completely gone and the pinhole vision of the left eye was 20/30—. On August 14th, the refraction without cycloplegia was: R.E., +0.25D. sph., 20/13; L.E., +2.5D. sph., 20/25. The media were now clear. The left macular area was still elevated with yellow spots around it but the hemorrhages had disappeared.

On September 11th, the refraction was: R.E., +0.25D. sph., 20/13; L.E., +0.75D. sph., 20/13. Many spots of choroiditis had by now disappeared and those remaining were pale white. Glinting white spots were visible about the left macula.

On October 7th, the refraction reached its definitive status: R.E. +0.25D. sph., 20/13; L.E., +0.25D. sph., 20/13. Presbyopic addition, +1.75D.

Though the refraction and visual acuity of the left eye had at this time regained normality, a disturbed color vision and micropsia still persisted. A bronze statuette was seen as such with the right eye but looked silvery with the left eye. The left eye, however, passed the Ishihara tests but on the Young charts yellow was called "orange," green—"purplish-gray," red—"purplish," and blue—"green."

After the completion of four months' treatment, the bronze statuette presented the same appearance to each eye and each eye passed all the Young charts correctly. In comparing the vision of the two eyes the patient noted micropsia in the left eye but he was otherwise unaware of it and had normal stereoscopic vision. The micropsia measures about seven percent with size lenses and has remained unchanged. After ophthalmoscopy the left eye is also slower in recovering from the after-image. At the macula radiations of white scar tissue are visible in the underlying choroid but pigment accumulation is slight.

On January 8th, the patient was tested with the Vollmer patch and again gave the four-plus reaction noted before commencing treatment. When tested with the Amsler charts,<sup>18</sup> using in the trial frame a near correction for 30 cm. (the reading prescription plus 0.5D. sph), the right eye perceived no abnormality in central vision. To the left eye the foveal field was intact but not the area about it. On the nasal side a dense purplish-gray blur was noted and the neighboring lines were distorted; inferiorly, a lambda-shaped shadow was seen; superiorly, a reniform cloud; and temporally, a spot of dimness (fig. 1). The tension of the scar tissue in the parafoveal lesions probably spread apart the elements in the avascular fovea, thus accounting for the perception of micropsia.

The spectacular effectiveness of chemo-antibiotic therapy in healing this case of tuberculous choroiditis is worthy of record. Objectively, the successive stages of resolution were: disappearance of exudate, absorption of infiltration, and cicatrization with minimal scar. Subjectively, the restoration of visual acuity definitely preceded that of the color sense.

## CASE 2

A factory supervisor, aged 58 years, had noted for 12 days a visual haze in the left eye affecting the upper-temporal field which

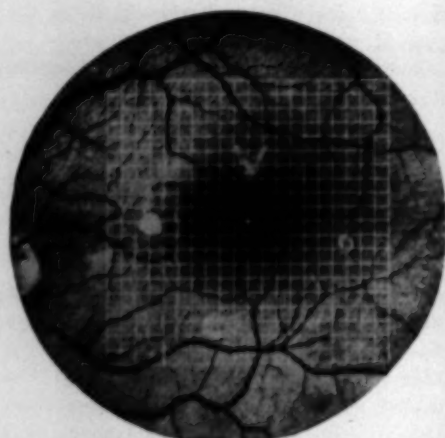


Fig. 1 (Lebensohn). The scotomas and distortions as seen by the left eye on the Amsler charts projected on the retina.

was particularly apparent when shaving. His glasses, procured only three months previously, tested: R.E., +1.0D. sph.  $\ominus$  +3.0D. cyl. ax. 120°, 20/25; L.E., +1.5D. sph.  $\ominus$  +3.5D. cyl. ax. 60°, 20/40 to 20/50 minus the left half of the test letters in each instance.

The ophthalmoscope showed a large splash of exudate just inferotemporal to the disc, streak hemorrhages above the adjacent inferotemporal vein, and a small round hemorrhage near the macula.

He had been affected since childhood with a chronic cough and poor appetite. Repeated chest X-ray studies had been consistently negative for tuberculosis. The blood Wassermann was negative. The reaction from the Vollmer patch test was three-plus.

In view of his history and the significance of a positive cutaneous tuberculin test at his age, the diagnosis of tuberculous choroiditis was made and chemo-antibiotic therapy instituted.

In 10 days the original exudate had disappeared except for a few scattered minute white spots. He ate and slept better and no longer was troubled by constipation. The reaction from the Vollmer patch persisted for over three weeks.

After one month's treatment the left eye had a corrected acuity of 20/25, but with the Amsler charts a cloud was seen in the 45-degree meridian and scattered breaks in the lines of the superior-temporal quadrant. Tests with Ishihara and Young charts showed normal color vision.

After two months' treatment no remains of exudate were ophthalmoscopically visible. Having developed a slight reaction to PAS, this drug was omitted for a week and he was instructed to use isoniazid and PAS on alternate days. At the third month of therapy, examination with the Harrington tangent screen showed no scotomas to white, blue, or red targets, but the Amsler charts disclosed a faint thin S-shaped cloud in the 35-degree meridian curving below toward the fovea, looking "like a gray erasure mark."

#### COMMENT

The chemo-antibiotic attack is unlikely to be of service in ocular tuberculosis of long standing in which irremediable destruction has ensued and in which the vascularity of the lesions is greatly reduced. I recently saw a physician-veteran with tuberculous iritis which had been treated for five years with tuberculin without avail and likewise failed to benefit from chemo-antibiotic therapy.

In a personal communication dated January 13, 1954, Irving H. Leopold states: "If there is suggestive evidence (of ocular tuberculosis), one can then try the combination of isoniazid, streptomycin, and *p*-aminosalicylic acid for a period of several weeks as a therapeutic test. If response occurs, then therapy should be continued for several months. If no response occurs, this may be evidence against the diagnosis of tuberculous etiology. . . . If one is going to treat choroiditis and believes it to be tuberculous, I certainly feel that all these drugs should be used. In this way the possibility of the development of resistant organisms will be markedly lessened."

In both experimental animals and man the clinical resolution of ocular tuberculosis by chemo-antibiotic therapy has not effected any change in the cutaneous tuberculin test. The skin-sensitizing antibodies or reagins are probably not involved directly in the processes of immunity. If desensitization with tuberculin has a value, its administration should be safer if preceded by adequate chemo-antibiotic therapy as by this means the hazards of focal reactions may probably be avoided.

4010 West Madison Street (24).

#### REFERENCES

1. Lepri, G., Capalbi, S., and del Vivo, E.: Chemotherapy in experimental ocular tuberculosis. *L'Année Therapeutique en Ophthalmologie*, **3**:479-508, 1952.
2. Goulding, R., and Robson, J. M.: Isoniazid in the control of experimental tuberculosis. *Lancet*, **2**: 849-853 (Nov.) 1952.
3. Pannarale, M. R., and Leonardi, F.: Effect of isoniazid on experimental ocular tuberculosis. *Boll. d'ocul.*, **32**:193-219 (Apr.) 1953.
4. Knapp, P., and von Sallmann, L.: Treatment of experimental ocular tuberculosis with isoniazid. *Am. J. Ophth.*, **36**:532 (Apr.) 1953.
5. Kratka, W. F., and Leopold, I. H.: Wills Eye Hospital Clinical Conference. *Am. J. Ophth.*, **36**:864 (June) 1953.
6. Bruna, F.: Action of isoniazid in experimental ocular tuberculosis. *Boll. d'ocul.*, **31**:527-546 (Sept.) 1952.
7. ———: Transfer and concentration of isoniazid into the aqueous of the rabbit. *Boll. d'ocul.*, **31**: 655-660 (Nov.) 1952.
8. Simonelli, M., and Rizzini, V.: Isoniazid in ophthalmology. *Gior. ital. oftal.*, **5**:293-303, 1953.
9. Alagna, G.: Isoniazid in ophthalmology. *Arch. di ottal.*, **57**:5-16, 1953.
10. Bard, E.: Tuberculous choroiditis. *Am. J. Ophth.*, **36**:990 (July) 1953.
11. Dolcet, L.: Tubercle of the optic papilla. *Arch. Soc. oftal. hispano-am.*, **12**:1418-1425 (Dec.) 1952.
12. Schlaegel, T. F., and Hungerford, L. N.: Isonicotinic acid hydrazide in ophthalmology. *Am. J. Ophth.*, **36**:537 (Apr.) 1953.



13. Borioni, D.: Experiences with isoniazid. *Boll. d'ocul.*, **32**:247-250 (Apr.) 1953.
14. Onfray, R., and Onfray, M. Uveal tuberculosis and atypical tuberculosis. *Bull. Soc. franç. ophtal.*, **63**:233-247, 1950.
15. Peric-Sajveit, F.: Tuberculosis of the choroid with retinal detachment. *Med. Arch.*, **3**:49-58, 1950.
16. Kapuscinski, W. J., and Drozdowska, S.: Diagnostic value of the Mantoux test in cases of inflammation of the mesenchymal tissue of the eye treated with vaccine. *Arch. d'ophtal.*, **11**:649-660, 1951.
17. Carr, D. T.: Current status of antimicrobial therapy in tuberculosis. *J.A.M.A.*, **150**:1170-1173, 1952.
18. Amsler, M.: Earliest symptoms of diseases of the macula. *Brit. J. Ophth.*, **37**:521-537, 1953.

## CALCIFIED SCLERAL NODULES IN HYPERVITAMINOSIS D\*

SAMUEL GARTNER, M.D., AND KARL RUBNER, M.D.

*New York*

Self-medication with vitamins is very popular and many think that a big dose is always better than a small one. This, however, is not innocuous.

Vitamin D in excessive dosage can cause acute intestinal disturbances of nausea, vomiting, and diarrhea. Chronic hypervitaminosis D may cause hypercalcemia and localized areas of pathologic calcification in various parts of the body. This has also been called metastatic calcification. Kidney impairment and stones are common and add to the disturbance. Calcification is frequent in some areas around the joints and in the blood vessels. The ocular complications, however, are less commonly noted.

Conjunctival and corneal opacities, some in the shape of band keratopathy, have been reported in cases of hypercalcemia by Meesman<sup>1</sup> in 1938, and later by Walsh and Howard,<sup>2</sup> Frost, et al.,<sup>3</sup> Cogan, et al.,<sup>4</sup> Fleischner and Shalek,<sup>5</sup> Gifford and Maguire.<sup>6</sup> In some of these reports, superficial conjunctival opacities near the limbus with a calcium density have been observed and in some cases demonstrated by X-ray studies. In one of the cases we studied, band keratopathy was present in a typical form.

Scleritis in rheumatoid arthritis has been the subject of a number of articles starting with Hothouse<sup>7</sup> in 1893, who reported a case with ulceration of the sclera. H. Friedenwald,<sup>8</sup> in 1921, reported arthritis and ne-

crosis of the sclera without perforation. In 1930, van der Hoeve,<sup>9</sup> who also quoted cases of Rochat,<sup>10</sup> called this syndrome "scleromalacia perforans." Verhoeff and King<sup>11</sup> suggested the name "necroscleritis nodosa excavans." Mundy, et al.,<sup>12</sup> as well as Ashton and Hobbs,<sup>13</sup> used the term "rheumatoid nodules of the sclera."

Histologic studies have also been reported by Smoleroff,<sup>14</sup> Harbater,<sup>15</sup> Anderson and Margolis,<sup>16</sup> and Goar and Smith.<sup>17</sup> In none of these cases has scleral calcification been noted. However, a number of the cases reported with hypervitaminosis D that showed calcification in the sclera were in cases of rheumatoid arthritis. One reason for this is that the arthritic patients have often been advised to take vitamin-D therapy. However, a patient with rheumatoid arthritis has a special tendency to scleral disease and, when this is complicated by hypervitaminosis D, scleral calcification may develop.

The two cases we studied contained certain similarities. One patient was aged 72 years, the other, 83 years. One had rheumatoid arthritis and both had consumed large doses of vitamin D and had hypercalcemia. Both had scleral nodules without ulceration. In one case, the eyes were obtained at autopsy. The scleral nodules had undergone considerable healing with the additional feature of calcification in portions of the nodules. Calcification in the sclera was demonstrated in the other case by X-ray films. She also had a band-formed keratitis.

\* From the Eye Service and Laboratory of Montefiore Hospital.



The histological study demonstrated many small scleral nodules. They were mainly anterior to the equator with the largest number over the ciliary body and the ora serrata. A few were further back with one over the macula. There was an increased number under the tendons of the recti muscles close to their insertion to the globe. The pull of the muscles on the sclera may have been a factor in this localization.

The nodules occupied only a small fraction of the sclera and extended to about one third to one half of the scleral thickness. Between them the sclera was normal. Their depth was variable, some superficial, but most of them were deep. It is very likely that much of the clinical differentiation between superficial and deep scleritis is artificial and not very important.

The typical nodule showed an area of necrosis with a low-grade inflammatory reaction, healing with newly formed vascularized connective tissue, and irregular calcification. In some nodules, giant cells were found around the necrotic area.

The scar tissue and the calcification are apparently a part of the healing process. The calcified plaque is not a source of irritation and does not provoke a cellular reaction.

Some of the nodules are in the deeper parts of the sclera in contact with the ciliary body or choroid. No appreciable inflammatory reaction was found in the uveal tract. In a few of the nodules there was adhesion of the choroid to the sclera. In others there was loss of pigment in the adjacent choroid.

In addition to the typical scleral nodules, there were a number of smaller calcified plaques at and around the limbus located just under the conjunctiva or protruding into it. These were densely calcified and in a few instances appeared to be in the early stages of bone formation. These lesions were different from the scleral nodules. There was no surrounding zone of necrosis or inflammatory reaction. This is probably the counterpart of the corneal and conjunctival le-

sions in hypercalcemia reported clinically by a number of authors.

#### CASE REPORTS

##### CASE 1

A white man, aged 72 years, a physician, had for the past 12 years attacks of pain in various parts of his body. Two years ago, he noted the development of nodules, mainly near the joints, which were painful at times. He took colchicine (four to five tablets daily) for some time. For the two years previous to his admission he had taken four to five potent vitamin-D tablets daily.

*Physical examination.* Blood pressure was 150/90 mm. Hg; pulse, 86; respirations, 16. He was an elderly, chronically ill man. Café-au-lait spots were noted on trunk and extremities. A Grade II systolic murmur was heard over entire precordium. The liver was enlarged to one finger below the costal margins. The prostate was symmetrically enlarged. There was limitation at many joints, which were the sites of large cystic or granular nodules (five to 15 cm. diameter). Neurologic examination was negative.

*Eye examination.* He had no eye complaints and the attending staff noted no abnormality of the eyes, so he was not referred to the eye department for examination.

*Laboratory data.* Admission, urine: Specific gravity, 1.010 (1.002-1.010), albumin trace (0-3+), some WBC and clumps. Culture: E. Coli and Staph. albus. Blood: Hemoglobin, 10.5 (615-10.5); WBC, 7,350 with 65-percent polys, 28-percent lymphs, five-percent eosinophils, and two-percent monocytes. Blood chemistry: BUN, 93.5; creatinine, 5.4; uric acid, 10.9; Ca, 12.3; P, 5.9. Analysis of skin nodule: Ca, 3.6 gm./100 cc.; uric acid, trace.

*X-ray report.* Generalized calcifications in soft tissues and joints with mild osteoarthritic changes.

X-ray films showed renal calculi with obstruction of the right ureter. Uretrosomy was performed for removal of the calculi and insertion of a catheter. He did well



Fig. 1 (Gartner and Rubner). Nodules in the sclera in the healing stage.  
(See also legend for Figure 2.)

after operation despite PSP excretion of 0% right kidney after two hours. He died of uremia on April 12, 1953.

#### AUTOPSY REPORT

The dura is partly calcified and has the consistency of an eggshell. Diffuse calcinosis was found in the subcutaneous tissue, dura, aorta, mitral and aortic valves, kidney, ureters, lungs, and thyroids. There was hydro-nephrosis, pyelonephritis, obstruction of right ureteropelvic junction, scar of right ureterostomy, secondary hyperparathyroidism, atrophy of bony trabeculae.

Café-au-lait spots are present over the extremities, numerous subcutaneous nodules, protruding from the skin, are distributed over back and extremities with predilection for the periarticular areas. They are extremely firm and range in size from 5.0 to 10 cm. in diameter. The joints were not involved and had normal synovial membranes.

The thyroid shows a distinctly enlarged and nodular right lobe. The left lobe is normal in size, shape, and consistency. On the anterior surface there are numerous nodules up to 0.5 cm. in size.

*Kidneys.* These organs are the site of an extensive pyelonephritis. Also present is a good deal of calcification.

*Dura.* This section is unusual in that there is intense calcification and at several sites there is a bony metaplasia.

*Parathyroids.* These glands are enlarged and pleomorphic in appearance. Some areas have diminished fat and hyperplasia of clear cells. Other areas have numerous water-clear cells arranged in nests and acini.

*Bone.* These sections reveal distinct thinning of the bony trabeculae but the marrow is normal in appearance.

#### CASE 2

This is the second admission to Montefiore Hospital of an 83-year-old white woman for investigation of a large mass in the right axilla. First admission was in October, 1952, for arthritis. History revealed intake of vitamin D (50,000 units, three times daily) for treatment of arthritis for several years prior to this admission. She was an obese woman with a strong suggestion of myxedema in her appearance.

*Eye examination.* Eye examination showed

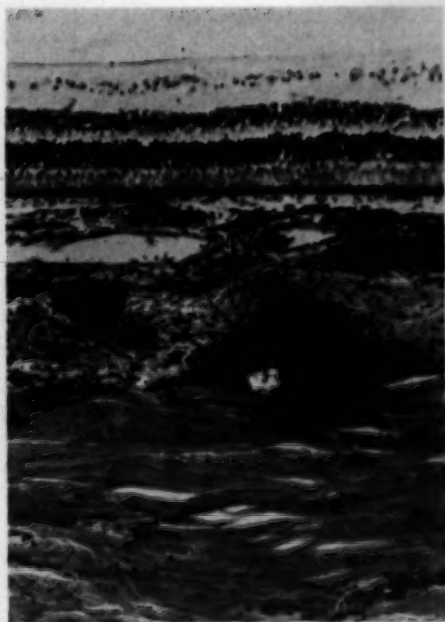


Fig. 2 (Gartner and Rubner). Nodules in the sclera in the healing stage. The lesions occupy about one third of the thickness of the sclera and are adjacent to the choroid. The scleral fibers have been replaced by newly formed vascularized connective tissue, some loose and areolar and some more densely cicatrized. There are irregular plaques of calcification. In Figure 1 there are giant cells and plasma cells. The sclera posterior to the lesions is partially necrosed with a loss of nuclei.



Fig. 3 (Gartner and Rubner). Nodule in the anterior part of the sclera in the deeper third adjacent to the ciliary body. A band of calcification is in contact with the ciliary musculature which is unaffected. On the outside of this band is an area of sclera devoid of nuclei with an irregular fibrillar arrangement which takes a bluish stain due to an increased calcium content.

band-form keratitis and numerous yellowish patches on the sclera. Bone-free X-ray examination with dental films proved these patches to have a calcium density. There was no history of previous scleritis, and the patient denied ever having had trouble with her eyes.

There were spoke opacities in both lenses. Vision seemed to be little affected, as the keratitis involved only the lower part of the cornea. Fundi were not remarkable and showed only narrowing of the vessels, consistent with her age, and arteriovenous nicking.

*Physical examination.* Blood pressure, 150/70 mm. Hg; pulse, 70. There were dilated veins over the right shoulder, a fixed

nontender hard mass in the right axilla. The lungs had a few basilar rales. Grade I systolic murmur. There was ankylosis of her knee joints. Calcification was seen in X-ray films of her right shoulder. Iodine<sup>131</sup> uptake was five percent.

*Laboratory.* Bone biopsy showed new bone formation and calcium deposition. Bone marrow normal. Hemoglobin, 8.5; WBC, 6,400 (normal differentiation); urine specific gravity, 1.008; albumin, two plus; sediment, WBC; PSP, six percent; 24-hour calcium excretion: 105.6 mg./24 hr.; serum calcium, 12 to 14.5; phosphorus 3.5 to 6.0; alkaline phosphatase, 3.0 to 4.9; TP, 5.9; BUN, 70 to 36; creatinine 4.6; X-ray examination revealed ectopic calcification.



Fig. 4 (Gartner and Rubner). Nodule in the sclera near the ora serrata. There is newly formed vascularized connective tissue with a moderate number of small round cells. There are a few giant cells in the periphery. There is no calcification in this nodule.

*Course.* The mass below the right clavicle was aspirated and calcified necrotic debris was found. Cystoscopy showed poor right

renal function. The patient's food intake gradually decreased and in spite of parenteral fluids her downward course continued. She died August 28, 1953.

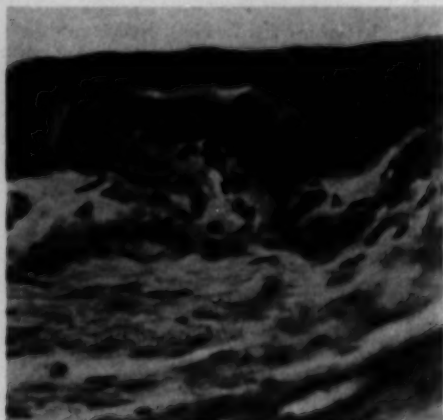


Fig. 5 (Gartner and Rubner). Calcified plaque in the conjunctiva near the limbus.

#### SUMMARY

Two cases of calcification in the sclera without ulceration are presented. Both patients had taken large doses of vitamin D and had hypercalcemia.

The eyes of one patient were obtained at autopsy. They demonstrated nodules in the sclera in varying stages of resolution with scleral calcification. Superficial calcified plaques in the conjunctiva were also demonstrated.

Calcification in the sclera was demonstrated in the other case by X-ray examination.

1749 Grand Concourse (53).  
103 East 86th Street.

#### REFERENCES

1. Meesman, A.: Hypokalzaemia und Linse. *Klin. Monatsbl. f. Augenh.*, **100**:1 (suppl.) 1938.
2. Walsh, F. B., and Howard, J. E.: Conjunctival and corneal lesions in hypercalcemia. *J. Clin. Endocrinol.*, **7**:644, 1947.
3. Frost, J. W., Sunderman, F. W., and Leopold, I. H.: Prolonged hypercalcemia and metastatic calcification of the sclera following the use of vitamin D in the treatment of rheumatoid arthritis. *Am. J. Med. Sc.*, **214**:639, 1947.

4. Cogan, D., Albright, F., and Barter, F. C.: Hypercalcemia and band keratopathy. *Arch. Ophthalm.*, **40**: 624, 1948.
5. Fleischner, F. S., and Shalek, S. R.: Conjunctival and corneal calcification in hypercalcemia. *New England J. Med.*, **241**: 863, 1949.
6. Gifford, E. S., and Maguire, E. F.: Band keratopathy in vitamin D intoxication. *Arch. Ophthalm.*, **52**: 106, 1954.
7. Holthouse, E. H.: An unusual case of ulceration of the conjunctiva and sclera. *Royal London Ophthalm. Hosp. Rep.*, **13**: 415, 1893.
8. Friedenwald, H.: Ocular conditions associated with arthritis deformans. *Am. J. Ophthalm.*, **4**: 431, 1921.
9. Van der Hoeve, J.: Scleromalacia perforans. *Arch. Ophthalm.*, **11**: 111, 1934.
10. Rochat: Quoted by Van der Hoeve.\*
11. Verhoeff, F. H., and King, M. F.: Scleromalacia perforans. *Arch. Ophthalm.*, **20**: 1013, 1938.
12. Mundy, W. L., Howard, R. M., Stillman, P. H., and Bevans, M.: Cortisone therapy in case of rheumatoid nodules of the eye in chronic rheumatoid arthritis. *Arch. Ophthalm.*, **45**: 531, 1951.
13. Ashton, N., and Hobbs, H. E.: Effect of cortisone on rheumatoid nodules of the sclera. *Brit. J. Ophthalm.*, **36**: 373, 1952.
14. Smoleroff, J.: Scleral disease in rheumatoid arthritis. *Arch. Ophthalm.*, **29**: 98, 1943.
15. Harbater, M.: Scleromalacia perforans. *Arch. Ophthalm.*, **41**: 183, 1949.
16. Anderson, B., and Margolis, G.: Scleromalacia. *Tr. Am. Ophthalm. Soc.*, **49**: 235, 1952.
17. Goar, E. L., and Smith, L. S.: Rheumatoid nodules of eye. *J.A.M.A.*, **148**: 889, 1952.

## TUBEROUS SCLEROSIS\*

### HISTORICAL REVIEW AND REPORT OF TWO CASES

WILLIAM JOACHIM PAGENSTECHE, M.D.

*Philadelphia, Pennsylvania*

Since tuberous sclerosis attracted the attention of the medical world in the second half of the last century, many authors have helped to establish the protean nature of this disease. More than 50 years, however, were required to work out the complete clinical picture with all its correlations.

Although our knowledge of the disease has increased, its occurrence is still rare. For this reason it seems pertinent to add the report of two cases to the already existing literature.

#### MANIFESTATIONS

Tuberous sclerosis, or Bourneville's disease, according to van der Hoeve,<sup>18</sup> is one of four different types of "phakomatoses." The other three types are von Recklinghausen's, Sturge-Weber's, and Hippel-Lindau's diseases.

These four clinical entities are more properly considered congenital syndromes than diseases, being often of familial or he-

reditary origin, and exhibiting different morbid localizations. The principal manifestations of tuberous sclerosis are pigment spots of the skin, and tumefactions and cysts in different parts of the body, especially in the nervous system. The lesions affect principally the brain (cortex, ventricles, white substance) and rarely affect the cerebellum and the medulla oblongata. Similar cysts are observed in the nerve-fiber layer of the retina and occasionally on the optic disc.

The skin of the face often presents adenoma sebaceum, which is almost 100 percent pathognomonic for the disease. The skin of the trunk and the extremities presents nevi, cafe-au-lait spots, and other pigmentary abnormalities, and tumors such as fibromas or lipomas.

Tumors may also occur in the heart (rhabdomyomas), kidney (cysts or hypernephromas), lungs, digestive tract, urinary bladder, thyroid, uterus, ovary, and other organs. Lesions may be present in the skull, vertebral column, and pelvic bone. Multiple

\*From the Department of Ophthalmology, Temple University School of Medicine.



defects and cysts may involve the iliac bone and neck of the femur, and may vary in size from that of a hazel-nut to that of a hen's egg.<sup>1</sup>

Other characteristics of the disease include: a hereditary tendency, a higher incidence in males, a high rate of stillbirths or death shortly after delivery, often with convulsions, and albuminuria in patients with far-advanced renal involvement. Other stigmas which have been noted are simian hand (flattening of the thenar eminence with inversion of the thumb and flexion of the terminal phalanx, often in association with *flexibilitas cerea*), asymmetries in the growth of the ears, high palate, spina bifida (eventually with ascending purulent meningitis),<sup>16</sup> ectopia testis, horseshoe kidney, patent ductus Botalli, and polydactyly or syndactyly.

#### VARIANTS IN THE CLINICAL PICTURE

The *full-blown* picture of tuberous sclerosis always includes brain involvement, along with involvement of the facial skin and possibly of the eyes. The skin of the body and one or more of the internal organs may also be affected.

In the *formes frustes* the picture is similar except that the brain lesions are minor and the localization is such that they produce no visible personality changes and allow apparently normal professional and social development. In fact, the *forme fruste* can be diagnosed only at autopsy. Here one may encounter, as an "incidental" finding, typical brain lesions in an individual who has been judged normal during his life.

Other patients, however, often in the same family, do not show brain involvement and are not classed as *formes frustes*. These cases are called monosymptomatic. Involvement may be present in only one site, such as sebaceous adenoma, kidney, or heart tumor, or pigment changes of the skin.

Thus we may find in families with phakomatotic tendencies of the Bourneville type all degrees of involvement from the full-blown epileptico-idiot to the person with

minimal skin lesions and normal intelligence who may even achieve a professional status of accomplishment. Between these two extremes, many different variations have been described.

The fully affected patient rarely lives more than 25 years, the duration depending on the localization of the disease process in the central nervous system. Death is frequently the result of status epilepticus or of intercurrent tuberculosis. Heart tumors, when present, usually develop early in life and result in sudden death long before mental manifestations become apparent; kidney tumors, which are not infrequently the cause of death, usually produce clinical symptoms of shorter or longer duration.

#### RELATIONSHIP WITH VON RECKLINGHAUSEN'S DISEASE

Bielschowsky, impressed by the many common features of von Recklinghausen's and Bourneville's disease, suggested that these two entities were the same process with different manifestations. He called attention to the close resemblance of the skin lesions, the close similarity of the cells in the brain lesions, a similar heredofamilial tendency associated with psychopathic trends, and the occurrence of retinal tumors in both conditions. The rare occurrence of epileptic attacks in some cases of von Recklinghausen's disease, as well as the occurrence of manifestations of both diseases in one patient, as reported by Orzechowski and Novicki,<sup>20</sup> seemed to support this idea.

Later Nieuwenhuys<sup>49</sup> stressed differences in the histology of the tumor cells, which are smaller and have less protoplasm in von Recklinghausen's disease than in Bourneville's disease. van der Hoeve,<sup>19</sup> moreover, commenting on the different behavior of the retinal tumors, noted the tendency to incrustation in von Recklinghausen's disease, and the tendency to vascular anomalies and cystic degeneration with retinal detachment and glial proliferation in Bourneville's disease. In essence, these authors showed that

these are two different entities belonging to the same group.

#### ETIOLOGY

Bourneville<sup>7</sup> considered the condition an inflammatory process (fetal encephalitis); Scarpatetti<sup>43</sup> attributed it to syphilis. Hartdegen,<sup>16</sup> in 1881, offered the neoplastic theory, which was later supported by Vogt<sup>38</sup> and Bielschowsky<sup>5</sup>—in contradiction to Alzheimer<sup>44</sup> and Bouwdijk-Bastiaanse,<sup>45</sup> who regarded the tuberous sclerosis as simple dysplasia, a process of malformation.

In an excellent paper on the histologic findings in the cases of van der Hoeve and De Fries, Feriz<sup>12</sup> attributes these multi-ocular lesions principally to exaggerated proliferations of a more or less differentiated atypical germinal and supporting tissue in the midst of, and replacing, functioning tissue.

#### HISTORICAL REVIEW

Historical description of tuberous sclerosis began on March 25, 1862, when the pathologist von Recklinghausen<sup>21</sup> showed before the Berlin Society of Gynecology the heart of a newborn infant which presented several prominent, partly outward, partly inward, tumors. The larger ones were in the wall of the ventricles, and one, situated in the left ventricle, was the size of a pigeon's egg. Being firmer than the myocardium, the tumors were well separated from the muscle but were not contained in a special capsule. The cut surface showed a paler red color than the muscle substance. von Recklinghausen's description of the cells is identical with that of rhabdomyoma. His article in *Verhandlungen der Berliner Gesellschaft für Geburtshilfe* ends: "The baby concerned died shortly after delivery, having taken several breaths. In the brain, in addition, a great amount of sclerosis (Sklerosen) was present."

In 1880, the French neurologist, Bourneville,<sup>7</sup> at Paris, described 10 cases of "a type of idiocy distinguished from other types of this disease by the presence of tuberous

changes in the cortex of the brain." He gave the name "sclérose tubéreuse des circonvolutions cérébrales" to this picture which, since then, has borne his name.

Independently of Bourneville's findings, the dermatologist Pringle,<sup>30</sup> in England, in 1890, described a case which showed efflorescences in the face with typical butterfly-shaped distribution over the nose and upper lip, to which he gave the name "sebaceous adenoma." This term had been first employed in a shorter communication of such a case in 1885 by Balzer and Ménétrier<sup>2</sup> from Paris. Pringle cited in his original paper five more corresponding cases observed at St. Louis Hospital in Paris, the site of Balzer's activity.

Pringle described in detail the characteristics of this skin lesion, which still bears his name, and drew the following classical conclusions:

1. The essential element is a hypertrophy of the sebaceous glands.
2. The site of predilection is the face, especially the parts of it where the sebaceous glands are normally present in greatest abundance.
3. The condition is always either congenital or observed in early life.
4. There is always a varying amount of concomitant vascular hypertrophy or telangiectasis.
5. Other degenerative or "nevroid" conditions of the skin are also often present (such as warts, true nevi, molluscum fibrosum, and pigment changes), the association being so frequent as to suggest a common cause.
6. The subjects of the disease appear to be, in general, intellectually below average, and all patients hitherto observed have been members of a low social order.

In 1908, the neurologist, Heinrich Vogt,<sup>38</sup> stated for the first time that the changes of tuberous sclerosis are often associated with adenoma sebaceum, which fact allowed him to make during life, a diagnosis of tuberous sclerosis that was later verified at autopsy. In the 19th century Bourneville, in his pri-

marily neurologic series (idiocy and epilepsy), had already noted dermatologic signs of the face in some of the patients, and Pringle, in his primarily dermatologic series (adenoma sebaceum), observed a reduced intelligence quotient in many of his group. However, it was Vogt who emphasized that appearance of sebaceous adenoma and Bourneville's disease in one and the same patient is not incidental—that indeed sebaceous adenoma is so closely related to Bourneville's disease as to be of pathognomic value in most cases.

The Berlin psychiatrist Berg,<sup>4</sup> in 1913, was the first to report the inheritance of tuberous sclerosis through three generations. The grandfather, normal mentally, died at the age of 60 years of a kidney tumor, very likely a hypernephroma. The father displayed sebaceous adenoma at four years of age; at the age of 20 years he had epileptic seizures, and he died at 21 years after removal of a tumor from the right kidney. Post-mortem examination of the brain by Kirpicznik showed a tuberous sclerosis vera. In the third generation a girl showed epileptic seizures at four years of age and died at the age of eight years. Autopsy showed extensive tuberosclerotic changes of the brain, with less involvement of the heart and kidneys. Berg's publication is interesting from the following points of view:

1. This family clearly presents, through three generations, hereditary traits and the tendency to anticipation, that is, the earlier appearance of the morbid signs, together with increased involvement in each successive generation.

2. Berg was the first to mention "eye complications" in two cases in which tuberous sclerosis was suspected. In the first case he noted "neuritic atrophy" in the right eye and several "choroiditis lesions" in the periphery of the left eye. His second patient showed "choroiditis lesions" in the periphery of both eyes.

Many specialties have contributed descriptions of part of the entire picture, which was

finally established by the ophthalmologist van der Hoeve<sup>18</sup> in 1921. van der Hoeve was the first to discern the true nature of the retinal lesions, recognizing them as being tumors originating in the nerve-fiber layer, and not sequelae of an inflammatory process. He called them "phakomata" (Greek *phakos*, the mother spot), as they are closely related to congenital moles. He observed that they may be progressive and may show cystic degeneration with possible rupture and hemorrhage.

Last, but not least, the roentgenologists reported roentgenologic signs in the various organs. Marcus,<sup>46</sup> in 1924, described characteristic changes in the skull of a patient with tuberous sclerosis. Dickerson,<sup>10</sup> in 1945 pointed out that some of these calcifications shown on roentgenograms of the skull are due to hyperostotic formations of the internal lamina, whereas others are apparently located in the brain itself.

As to the nature of these latter changes, Yakovlev,<sup>40</sup> in 1939, demonstrated two varieties of calcium deposits: (1) Those in the tuberosclerotic nests of the cortex, and (2) those in the spongioplastic tumors in the ventricles.

Ackermann,<sup>1</sup> in 1938, described the presence of extensive cysts in the neck of each femur. Berg and Vejlens<sup>47</sup> observed cyst formation of both lungs in a 32-year-old mentally normal female, with multiple tuberosclerotic changes observed at autopsy. A similar pulmonary condition was found in her sister.

Some authors<sup>1, 48</sup> consider that these osseous manifestations may represent functional alterations due to neuroendocrine and neurovascular disorders caused by the involvement of the hypothalamus and the vegetative nervous system. Others<sup>28, 40</sup> attribute them to developmental disorders in the mesoderm (dysplasia of embryonal tissue).

#### CASE REPORTS

The two cases reported here are of interest; the first because of the clinical mani-



Fig. 1 (Pagenstecher). Case 1. The patient at the age of nine years, showing a full-blown case of Bourneville's disease.

festations, and the second because of the autopsy findings.

#### CASE 1

*Clinical history:* William St. (fig. 1), the main subject of this study, was hospitalized for the sixth time on January 26, 1954, at the age of nine years.

William was born January 6, 1945, and, according to the mother, was more than one month postmature. At birth the infant weighted over nine pounds, and was "all grey." Soon after birth episodes were noted of "stiffening of the body" and "rolling of the eyes." These spells originally lasted no longer than one or two seconds, and different consultants attributed them to "temper" or to "teething." At the age of nine months, hospital observation was non-revealing as to etiology, and no diagnosis was made.

At the age of one year the boy had spells of longer duration and greater frequency (four to six daily), and was found to be retarded, with some athetoid movements and weakness of the right arm, attributed by the pediatrician to a cortical deficiency.

*Air encephalography* revealed a definite filling defect in the left ventricle, slightly anterior to the junction of the body and posterior horn. The child was again hospitalized.

*Trephining* revealed a normal amount of subdural fluid, with normal intraventricular pressure. The cortex, however, appeared atrophic, and it was noted that there was an "abnormal feeling" as the cannula penetrated the ventricle. Discharge diagnosis was "cerebral agenesis."

The child first sat up at 17 months of age, and learned to walk at 22 months. A third hospitalization at the age of five years led to the diagnosis of "mental retardation of unknown etiology." Eye examination at this time was negative. The patient was then transferred to a cerebral palsy clinic, where electroencephalography (August 16, 1950) suggested a convulsive focus in the right motor region. Repeated roentgenograms of the skull (1950, 1951) revealed a single calcification in the right hemisphere.

At the age of six years the child was again hospitalized (May 25 to June 9, 1951) for air encephalography. The ventricular system was found to be within normal limits, but electroencephalography was reported as follows:

"The child was examined while awake and restless. The record showed slow and sharp waves in all leads. No evidence of a focal lesion is seen. The dart-and-dome pattern characteristic of petit mal is not noted. Spontaneous hyperventilation was followed by a typical seizure during which the pattern was accentuated but not changed. Impression: cerebral dysrhythmia."

At this time the child was having many attacks of petit mal, although there were no clonic convulsions. Despite sedation with Tridione and phenobarbital, the attacks became progressively worse. The child could not talk, but supposedly understood simple instructions; about all he did was rock from morning to night. He hyperventilated a great deal, especially when excited.

Lesions suggestive of adenoma sebaceum had developed on the face during the preceding months, which the dermatologist described as "a number of pinhead-sized yellowish-brown papules on both cheeks, which also show fine telangiectases. Some of these measure a few millimeters in diameter and have a verrucous appearance. The distribution is typically butterfly-shaped." (fig. 2.)

Furthermore, of interest to the dermatologist, was an area of vitiligo (2.0 by 0.5 cm.) present on the right cheek, and a few small areas of vitiligo,



Fig. 2 (Pagenstecher). Case 1. When hospitalized at the age of six years the patient showed lesions, suggestive of adenoma sebaceum, which had developed on the face during the preceding months.





Fig. 3 (Pagenstecher). Case 1. Two areas of vitiligo were present on the back of the right leg.

scattered on each leg (fig. 3). A small, slightly elevated plaque (1.0 by 0.5 cm.) in the right inguinal region was considered to be a fibroma.

*Psychometric evaluation* showed the child to be functioning at the level of an infant. Vision and hearing were satisfactory; the pupils retracted to light; the eardrums were normal. The palate was high and arched; the front teeth were ground down, and there were a large number of carious lesions. Heart, lungs, and abdomen were within normal limits; testes were descended and genitalia were normal for the age.

*Neurologic examination* showed no focal lesions.

*Serologic examination* was negative. Hemoglobin was 14.6 gm./100 cc. white blood cells, 5,900; neutrophils (segmented) 43 percent, (nonsegmented) five percent. Urinalysis was negative except for trace of acetone; phenylpyruvic acid was negative.

These findings clearly established that this was not a case of cerebral palsy, and the diagnosis of tuberous sclerosis was made. Institutionalization of the child was recommended.

On year later a status convulsivus developed, and the patient was admitted for the fifth time (November 24 to December 4, 1952) for control observation.

*Physical examination* at this time revealed a well-nourished white boy with generalized tonic and clonic convulsions. Blood pressure was 100/60 mm. Hg; pulse, 100; respirations, 28; temperature 98.2°F. The patient was unconscious and responded only to deep pin-prick. There was questionable weakness of the right arm and leg, with increased tendon reflexes on the right side and bilateral Babinski. There were no other significant physical findings.

*Fundus examination* revealed no pathologic changes. Urinalysis was negative. Total carbon dioxide was 25.9 vol. percent; chlorides, 110 mg. percent; and potassium, 4.95 mg. percent. Spinal fluid was clear, with three white blood cells, 60 mg. of protein, and 63.5 mg. of sugar; spinal-fluid culture was negative.

*Roentgenograms* of the chest and of the hands and feet were negative. Roentgenography of the skull (November 28, 1952) revealed an oval calcific density inside the cranial vault, approximately

four cm. above the sella turcica and slightly to the right of the midline, apparently localized in the region of the right thalamus. Its shape and position had not changed since the examination two years earlier (September 13, 1950). A radiolucent defect, representing a burr hole from a previous operative procedure, was apparent in the left parietal bone. A mottled area of sclerosis was noted in the left parietal bone, approximately one cm. behind the burr hole defect (fig. 4.) No other intracranial calcifications were seen; subarachnoid channels were normal, and skull measurements were within normal limits.

The patient was brought under control with 90 mg. of sodium phenobarbital subcutaneously, and with this regime he had no further convulsions. On discharge institutionalization was again recommended.

Some time after discharge, despite high doses of sodium phenobarbital, lightning seizures again occurred, averaging three to five major attacks daily.

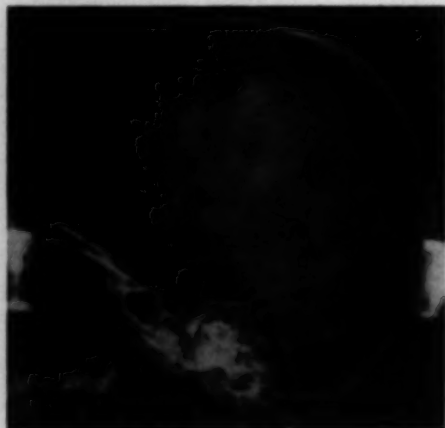


Fig. 4 (Pagenstecher). Case 1. A skull X-ray film taken on November 28, 1952, showed a mottled area of sclerosis in the left parietal bone.



At the end of 1953, the patient had regressed markedly, with major and minor attacks occurring as frequently as 50 an hour. This led to the sixth admission, at the age of nine years, on January 26, 1954.

*Physical examination* at the time of this admission revealed general deterioration of the patient, with greater inability to walk, greater convulsions, and incontinence for urine, feces, and saliva.

Head size at this time was 19.5 cm. Diffuse adenopathy was noted along the anterior cervical chain, and there was spasticity of the right arm.

*Dental examination* revealed bleeding from hypertrophic gingiva and possible mild scurvy.

*The ophthalmoscopic examination* revealed an apparently good vision. Both eyes were externally normal, with no limitation of movement and no nystagmus. Corneal sensitivity was normal. The pupils were equal (three mm. in size). They reacted promptly to light and accommodation. The media were clear, and the tension in each eye was 18 mm. Hg (Schiotz).

Each fundus, on ophthalmoscopic examination, revealed a normal papilla with sharp outline and no elevation of the surface. There were no drusen-like changes or crests. Foveal reflex was normal.

In the temporal upper quadrant of the left eye, some two disc diameters away from the optic-nerve head, an oval tumor mass, 1.0 by 2.0 disc diameters in extension and grayish-white in color was visible. The mulberrylike surface of the mass was elevated some two to three diopters above the level of the surrounding retina. The upper border of the mass was limited by the superior temporal artery, which showed sheathing shortly after leaving the nerve head. The superior temporal vein ran straight through the tumor. This vein, and some smaller tributaries could be seen shimmering through in its entire "intratumoral" course. This tumor in all its detail, closely resembled that reported by Reese in 1940.

Examination under general anesthesia revealed three additional flat, circular, grayish-white growths of minimal prominence. Two of them were closely connected with the inferior temporal vessels, and the third, smallest growth, was in the superior nasal quadrant, without apparent vascular connection. These three growths appear closely related to those described by van der Hoeve in 1921. A Kodachrome photograph of the larger lesions was obtained, but the smaller lesions, situated more peripherally, escaped the camera lens.

Figure 5, based on the photograph and the studies made with the patient under general anesthesia, reveals the entire story. Subsequent observations revealed no change in these masses.

The periphery of the right eye was without pathologic changes.

A petit mal seizure, lasting some 20 seconds, was noted the first day, with rigidity of the body and trembling of the arms and legs. A typical grand mal seizure, lasting two and one-half minutes, oc-

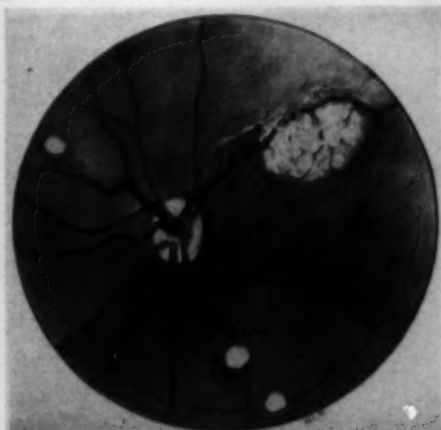


Fig. 5 (Pagenstecher). *Case 1.* A fundus drawing based on a photograph and studies made with the patient under general anesthesia, showing four tumor masses in the left eye.

curred the second day, with rigidity, foaming at the mouth, tongue biting, and slight generalized twitching, but without incontinence or cyanosis. The patient was put under heavy sedation, with 400 mg. Dilantin and 30 mg. sodium phenobarbital, four times daily (Putnam regime), and the convulsions very quickly stopped.

The patient was discharged on February 11, 1954, after nine days without seizures.

*Family history* (fig. 6). The paternal grandfather of this patient died at the age of 74 years as a result of "kidney trouble." He reportedly had no "spells," was of "normal" intelligence, and was active as a barber until his death.

Of six children born in the second generation, two—the third and the fourth born—died with convulsions before the age of six months. The oldest son, now a widower, has five normal children. The youngest two, sisters, are said to have had "spells" as children, but these ceased in later life. Both are now married, and the older of the two has children. All these living siblings are apparently of "normal" intelligence; the younger sister is a school teacher.

Unfortunately, none of these persons have been available for examination to determine the possible presence of minor stigmas of Bourneville's disease, such as pigmentary or tumorous disorders of the skin, or psychopathic trends, such as absences, emotional instability, and intellectual defects, with the usual tendency to rapid deterioration at or before puberty.

William's father, the second son in the above-described group, works as a plumber at the Navy yard. He is apparently in good health and annual medical examinations by his employer have revealed no gross abnormalities. Our special survey

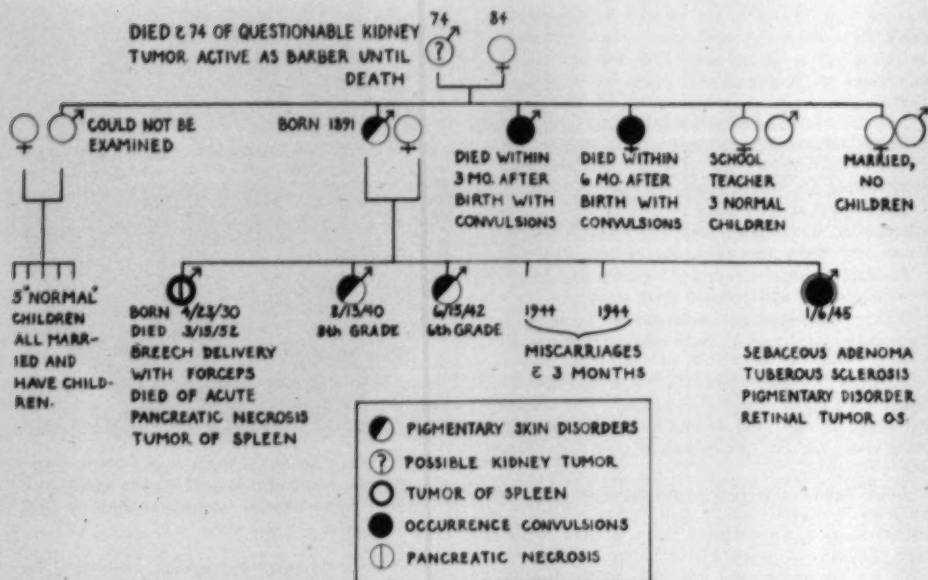


Fig. 6 (Pagenstecher). Case I. Pedigree of the family.

reveals three pigmented nevi, each about the size of a dime, on the left temple. A skin tumor, 2.0 by 1.0 by 0.5 cm., on his right forehead is apparently a lipoma. His vision is: R.E., 6/6, with a -1.5D. sph. -3.0D. cyl. ax. 180°; L.E., 6/7, with a -1.25D. sph. -2.5D. cyl. ax. 180°.

William's mother has an apparently healthy family background. Her examination reveals no abnormalities. Her vision is: R.E., 6/6, with a -1.0D. cyl. ax. 105°; L.E., 6/6, with a -0.5D. sph. -1.5D. cyl. ax. 60°.

Bernard, William's oldest brother, was delivered by forceps from a breech presentation. Subsequent development was normal. He died suddenly, at the age of 21 years, while serving in the Navy. The primary pathologic diagnosis at autopsy was "acute pancreatic necrosis." The autopsy report read, in part:

"The pancreas is normal in size. It is soft to the point of liquefaction, especially in the body. It is markedly hyperemic, with hyperemia not extending past the capsule. Some lobules are preserved. There is no evidence of calculi of the ducts."

Secondary pathologic diagnoses were: edema and hyperemia of the brain, and splenomegaly (335 gm.). There was an accessory spleen, two cm. in diameter.

The autopsy report does not mention scleroses of the cortex or of any other viscera, or any dermatologic abnormality. The only finding of this report which has been described in other cases of tuberous sclerosis is the splenoma.

Two other brothers, Robert (aged 13 years, in

the eighth grade) and Donald (aged 11 years, in the sixth grade), were normal infants, delivered spontaneously at term. Both had the usual childhood diseases but, besides being "nervous," presented no abnormalities. However, complete examination at this time reveals multiple pigmentary disorders of the skin of the trunk and lower extremities.

Robert has a café-au-lait spot (1.0 by 0.5 cm.) on the left lower abdominal quadrant and multiple spots on the back of increased or decreased pigmentation. Donald has a café-au-lait spot (2.0 by 0.5 cm.) under the left buttock and some "goose-flesh" changes of the skin over his sternum—this is a variant type of fibroma in which large numbers of miliary fibrous tubercles are scattered over the skin in certain areas of the trunk. These slightly raised papules, smaller than a pinhead and indistinguishable in color from the surrounding skin, resemble in size and appearance, coarse "goose-flesh."

Robert's vision is: R.E., 6/6, with a -0.5D. sph. -0.75D. cyl. ax. 175°; L.E., 6/7, with a -0.5D. sph. -0.75D. cyl. ax. 175°.

Donald's vision, without prescription, is 6/6 for both eyes.

During 1944, two years after Donald's birth, the mother had two miscarriages, each at the beginning of the second trimester of gestation. The following year William was born.

#### COMMENT ON CASE 1

Regarding the pedigree of this family from the point of view of tuberous sclerosis,



Fig. 7 (Pagenstecher). Case 2. Photomicrograph ( $\times 10$ ) of a nodule situated under the endocardium (hematoxylin-eosin). Note the apparent sharp transition from normal surrounding cardiac fibers to vacuolated cells.

we note:

In the first generation the grandfather died of "kidney troubles" which fact is remarkable as we know that kidney tumors arise in 80 percent of tuberous sclerosis cases. Berg published a similar case in which the mentally healthy grandfather developed a left-sided kidney tumor (verified by laparotomy) in older age. As there is no proof by laparotomy or biopsy, this diagnosis must in the present case remain at best an assumption. It is, therefore, marked with a question mark.

In the second generation, the only manifestations present in the patient's father are tumorous and pigmentary disorders of the skin. The two siblings born after him died of convulsions within a few months after

birth. Such early death, associated with earlier appearance and increased severity of symptoms, or stillbirths, are common in families with known tuberosclerotic tendencies.

In the third generation, the trends of the disease, which had been masked before, show up much more clearly. There is a history of two miscarriages. Two children (Robert and Donald) have skin manifestations, and there is one full-blown case of Bourneville's disease (William), with: (1) Idiocy, (2) epileptic spells, (3) morbus Pringle, (4) retinal phakoma, (5) cerebral calcifications, (6) various pigmentary and tumorous disorders of skin of trunk and extremities, (7) high palate, (8) motor restlessness, (9) right hemiparesis, (10) gross impairment of

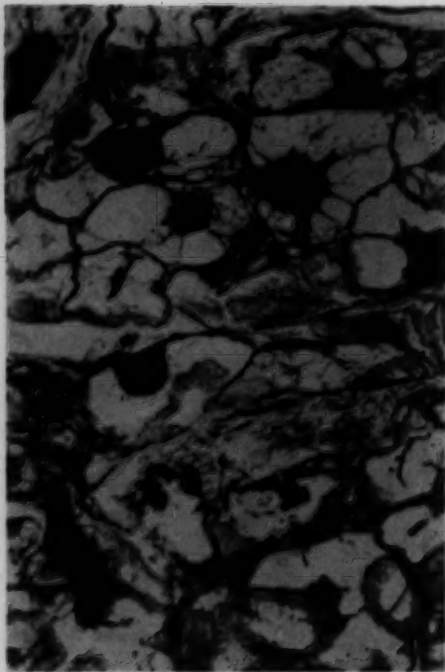


Fig. 8 (Pagenstecher). Case 2. Photomicrograph of a tumor nodule under higher magnification ( $\times 267$ , hematoxylin-eosin). Note the presence of numerous spider cells and large spaces. The former show central location of the nucleus and the delicate cytoplasmic strands in a spider-web arrangement. The latter are filled with glycogen.

speech, (11) liveliness in tendon response on right, (12) tendency to hand-finger play (fig. 1), (13) progressive nature of clinical picture, with remissions, and (14) inheritance.\*

When reviewing William's history we note that, at two previous ophthalmoscopic examinations, no pathologic findings were reported. This raises the following questions:

1. Did the phakomas in the left eye de-

\* Knowledge of the hereditary nature of the disease has led some writers to prohibit marriage between members of families with known history of tuberous sclerosis, and to recommend contraception for couples in which one partner comes from such a family (Ley<sup>41</sup>).

velop in the two years since the last negative funduscopy in 1952?

2. Have they been present for more than two years or ever since birth and were they simply overlooked during the difficult examination of the restless boy?

At first one might think that the size of the larger lesion would be more in favor of the second possibility. Observations in the literature, however, note that the skin lesions are usually not present at birth and do not occur before several months or years afterward. This fact seems to justify the assumption that the same might be true for the intraocular lesions. van der Hoeve's<sup>18</sup> case, which showed marked growth and even cyst formation during consecutive studies, might probably also give some support to this idea.

Bernard, the oldest son, who died suddenly at the age of 21 years, attracts our special interest, the question arising whether the pancreatic necrosis found at autopsy was in any way connected with tuberous sclerosis. Review of the literature revealed no mention of the pancreas among the manifold internal organs involved. However, van der Hoeve<sup>22</sup> did report occurrence of pancreatic cysts in von Recklinghausen's disease.

In view of the close relationship between the two syndromes, the following questions might be raised:

1. May involvement of the pancreas, or pancreatic duct, occur in extremely rare cases of tuberous sclerosis? Might this case be one of those?

2. Could sudden change in such a hypothetical lesion, like rupture of a cyst or obstruction of a small duct, have caused the acute necrosis, while the quick digestion of the tissues by the pancreatic enzymes destroyed all the histologic traces of the causative mechanism?

3. Was this just a coincidental occurrence of pancreatic necrosis "sui generis" in a member of a family with tendencies toward tuberous sclerosis?

Unfortunately, neither the autopsy findings nor the literature can give us any definite answer. With our present knowledge, we

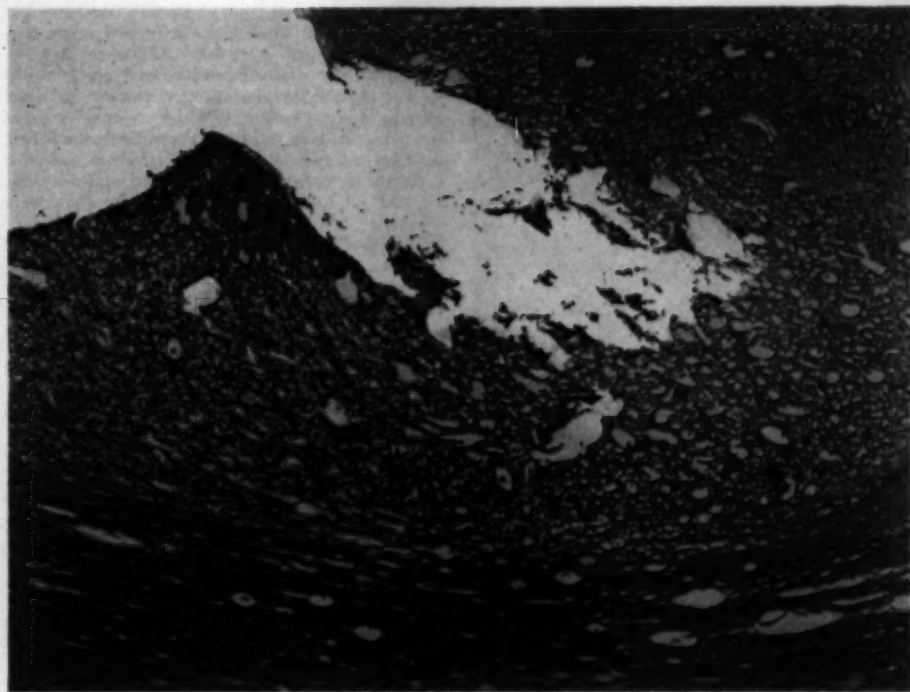


Fig. 9 (Pagenstecher). Nodule in the cortex ( $\times 26$ , hematoxylin-eosin).

must assume the third possibility to be the most likely. Nevertheless, this is the first report of the occurrence of acute pancreatic necrosis in a sibling of a family with Bourneville's disease, and the question, once raised, can probably be elucidated in future cases.

As to the accessory spleen, mentioned secondarily in Bernard's autopsy report, such anomalies have been described in patients with tuberous sclerosis. However, since such a splenoma frequently occurs in completely normal individuals, it certainly cannot, especially when occurring alone, be evaluated as a stigma of tuberous sclerosis.

#### CASE 2

*Clinical history.* A. L., a boy, aged two years, with the family history unknown, was said to have been born as a breech. The weight at birth was reported as nine lb., four oz. He walked at 18 months with a staggering gait, limping on the left leg as though it was shorter. He never talked. Convulsions first appeared at the age of three months and had

continued at intervals. Upper respiratory infection seemed to predispose to more frequent attacks.

On admission in April, 1939, he was a low-grade imbecile with retarded co-ordination of movement.

*Air encephalography* showed considerable dilatation and symmetrical filling of the ventricles. There was a bumpy appearance of the inner surface of the ventricles, suggestive of tuberous sclerosis—among several other diagnostic possibilities.

Several days after this procedure the temperature rose to  $103^{\circ}\text{F}$ ., with a pulse rate of 160 and a respiration of 64. There was some photophobia, nuchal rigidity, restlessness, and a suggested bilateral Kernig and Brudzinski. The chest examination was negative.

A diagnosis of meningitis was made at this time. A lumbar puncture was done, and cloudy cerebrospinal fluid was removed. The study of the fluid revealed innumerable leukocytes, polymorphonuclears predominating. Culture of the spinal fluid resulted in growth of many influenza bacilli. A blood count on May 11, 1939, revealed 37,000 W.B.C. with 80 percent polymorphonuclears and only 12 percent lymphocytes.

Conditions gradually became worse and the child died on May 29, 1939.

*At post-mortem examination* the body of a fairly well-developed, somewhat undernourished white





Fig. 10 (Pagenstecher). Giant cells in the cortex ( $\times 253$ , hematoxylin-eosin).

male child was seen with an apparent age of about two years. The weight of the body was 26 lb. The heart weighed 100 gm. The epicardial surface was smooth and glistening.

The myocardium appeared somewhat thicker than would be expected for a child this age, especially the left ventricle.

On the endocardial surface of the left ventricle, just beneath one of the aortic cusps, is a small, slightly raised, yellowish area measuring about five mm. in diameter. The valves all appear competent. On the endocardial surface of the left ventricular cavity a bulge into the cavity near the apex of the heart is noted. This is moderately firm and considerably raised above the surrounding area. Section through this portion revealed a circumscribed mass of moderately firm, whitish-gray tissue measuring about one cm. in diameter.

Section through the interventricular wall revealed a similar lesion somewhat smaller in size. Numerous sections through the myocardium in various portions of the heart revealed several smaller, well-demarcated whitish lesions similar to the above. The aorta appeared grossly normal.

The right kidney weighed 80 gm. and the left 75 gm. Multiple small cystic cavities were scattered over the entire cortical surface of both kidneys.

These varied in size from about three mm. to eight mm. in diameter. The capsule stripped fairly easily, rupturing a good many of the superficial cysts. Several small whitish areas were present in the intervening kidney structure. On section the cystic cavities were scattered diffusely throughout the entire kidney, being about as numerous in the deeper structure as they were on the cortical surface. The ureters were patent, the bladder was negative. Gall-bladder, bile ducts, pancreas, intestinal tract were normal.

Over the entire base of the brain, but especially about the upper cervical cord, the medulla, pons, and upper brain, there was thick plastic membranous gray-yellow exudate which completely covered and masked the origins of the nerves as well as the vessels of the brain. This exudate seemed to be almost entirely confined at the base especially below the tentorium.

Coronal sections through this brain showed a dilatation of the lateral ventricles. These lateral ventricles were filled with a soft greenish-gray purulent material. The walls of the ventricles had a nodular appearance, some of them measuring 1.5 cm. high and 1.0 cm. in diameter. Nodular portions were extremely firm and white; their surfaces were smooth and glistening.

Throughout the entire cerebrum, there were multiple plaquelike nodules to be felt, especially in the cortical region. These were of varying size; the edges were not particularly discrete. The cut surface was homogeneous, the consistency was extremely hard. In the regions where the nodules were apparent, the cortex faded out and became indistinguishable from the white matter. This gave the peripheral portions of the sinuses a curious mottled appearance with, in some places, a cortex of normal color and thickness and, in others, the white matter extending to the edge of the section.

*Anatomic diagnosis.* Influenza meningitis, tuberculous sclerosis, rhabdomyomas of the heart.

#### *Microscopic examination*

*Heart.* Histologic preparations of the nodules stained with hematoxylin-eosin presented the typical vacuolated appearance described in the literature (Batchelor and Maun<sup>80</sup>). The boundaries were for the greater part sharp and at some places more gradually transient (figs. 7 and 8). They were composed largely of cells with striated fibrils of a primitive type, varying from 8.0 to 300 microns in diameter. Staining with Best's carmine method revealed numerous glycogen granules in the vacuoles.

*Brain.* Sections of the brain (hematoxylin-eosin stain) showed a marked degree of gliosis—most pronounced in the molecular layer of the cortex. A second feature was the disturbance of the architecture of the cortex—most pronounced in the layer of the small and middle pyramidal cells (figs. 9 and 10). In the center of the bigger lesions the normal arrangement of the layers was completely disintegrated.

The ganglion cells, diminished in number, were

displaced and showed an atypical and protean shape. The occurrence of atypical giant cells was characteristic (fig. 10). These were far larger than the biggest pyramidal cells. Some of them with bigger triangular nuclei looked like atypical ganglion cells while others with smaller eccentrically located nuclei seemed to be more glial in nature. A third type had no apparent relation with either cell type.

#### COMMENT ON CASE 2

This case is of interest because of the relative rarity of the rhabdomyomas. Up to 1931, only three cases had been described in the American literature. Those were followed by 11 more during recent years, so that this case brings the total number to 15.

This patient was admitted for air-ventriculography because of an unclear convulsive status. The X-ray findings of the brain first aroused suspicion of tuberous sclerosis which

was later confirmed by the autopsy findings.

#### SUMMARY

In this paper, the syndrome of tuberous sclerosis, has been discussed from various aspects, including: (1) Manifestations, (2) historical review, (3) presentation of a clinical case with familial involvement, and (4) presentation of a second case with demonstration of the histologic findings of brain and heart.

The following questions have been raised:

A. Is involvement of the pancreas by tuberous sclerosis possible in rare instances?

B. Is it possible for marked retinal phakomas to develop in a period of two years?

Temple University Hospital (40).

#### REFERENCES

1. Ackermann, A. J.: Pulmonary and osseous manifestations of tuberous sclerosis with some remarks on their pathogenesis. *Am. J. Roentgenol.*, **51**:315, 1944.
2. Balzer, F., and Ménétrier, P.: Étude sur un cas d'adénomes sébacés de la face et du cuir chevelu. *Arch. de physiol.*, **6**:564, 1885.
3. Bau-Prussakova, S.: Ueber einen Fall von tuberoeser Hirnsklerose mit Netzhautveraenderungen und benignem Verlauf. *Ztschr. f. d. ges. Neurol. & Psychiat.*, **145**:275-282, 1933.
4. Berg, H.: Vererbung der tuberoesen Sklerose durch 2-3 Generationen. *Ztschr. f. d. ges. Neurol. & Psychiat.*, **19**:528-539, 1913.
5. Bielschowsky, M., and Gallus: Ueber tuberoese Sklerose. *J. f. Psychiat. & Neurol.*, **20**:1, 1913.
6. Bloch, F. J., and Grove, B. A.: Tuberous sclerosis with retinal tumor: Report of a case. *Arch. Ophth.*, **19**:34-38, 1938.
7. Bourneville, D.: Contribution a l'étude de l'idiotie; idiotie et épilepsie hémiplegique. *Arch. de Neurol.*, **1**:81, 1880-1881.
8. Braun, W.: Familial occurrence of drusen (hyaline bodies) in the optic nerve. *Klin. Monatsbl. f. Augenh.*, **94**:734-738, 1935.
9. Critchley, M., and Earl, C. J. C.: Tuberoese sclerosis and allied conditions. *Brain*, **55**:311-346, 1932.
10. Dickerson, W. W.: Characteristic changes associated with tuberous sclerosis. *Arch. Neurol. & Psychiat.*, **53**:199-204, 1945.
11. Féré et Mouroux: Note sur la fréquence et sur la distribution des naevi chez les aliénés. *Arch. Neurol.*, **18**:105, 1889.
12. Feriz, H.: Ein Beitrag zur Histopathologie der tuberoesen Sklerose. *Arch. path. Anat.*, **278**:690, 1930.
13. Fischer: Die Nierentumoren bei der tuberoesen Hirnsklerose. *Beitr. z. path. Anat. u. allg. Path.*, **50**:235, 1911.
14. Globus, J. H., and Selinsky, H.: Tuberoese sclerosis in the infant. *Am. J. Dis. Child.*, **50**:954-965, 1935.
15. Guillaïn and Lagrange: Phacomatose rétinienne de van der Hoeve dans un cas de sclérose tubéreuse. *Bull. et mem. Soc. méd. d. hôp. de Paris*, **50**:1421-1425, 1934.
16. Hartdegen, A.: Ein Fall von multipler Verhaertung des Grosshirns nebst histologisch eigenartigen harten Geschwuelsten der Seitenventrikel (Glioma gangliocellulare) bei einem Neugeborenen. *Arch. f. Psychiat.*, **11**:117, 1881.
17. Herrenschiwand: Ueber Augenhintergrundsveraenderungen bei tuberoeser Hirnsklerose. *Klin. Monatsbl. f. Augenh.*, **48**:732-736, 1929.
18. van der Hoeve, J.: Augengeschwuelste bei der tuberoesen Hirnsklerose. *Arch. f. Ophth.*, **105**:880-889, 1921.
19. ———: Augengeschwuelste bei der tuberoesen Hirnsklerose (Bourneville) und verwandten Krankheiten. *Arch. f. Ophth.*, **111**:1-16, 1923.

20. ———: Eye diseases in tuberose sclerosis of the brain and in Recklinghausen's disease. Tr. Ophth. Soc. U. Kingdom, **43**:534-541, 1923.
21. ———: Eye symptoms in phakomatosis. Tr. Ophth. Soc. U. Kingdom, **52**:380-401, 1932.
22. ———: Les phakomatoses de Bourneville, de Recklinghausen et de v. Hippel-Lindau. J. belge neurol. et psychiat., **33**:752-762, 1933.
23. Koch, F. L. P., and Walsh, M. N.: Syndrome of tuberose sclerosis: Report of a case. Arch. Ophth., **21**:465-475, 1939.
24. Kuchenmeister: Ueber einen Fall von Pringle'scher Krankheit mit Veraenderungen am Augenhintergrund und an der Schleimhaut von Blase und Mastdarm. Dermat. Wchnschr., **99**:1333-1337, 1934.
25. Kveim, A.: Ueber Adenoma sebaceum (Morbus Pringle), und seinen Platz im neurokutanen Syndrom—tuberose Gehirnsklerose—und dessen Beziehungen zur v. Recklinghausen'schen Krankheit. Drei Faelle von tuberose Sklerose und Morbus Pringle mit roentgenologisch nachweisbaren Veraenderungen im Knochensystem, und Tumorbildungen. Acta dermat. & venerol., **18**:637, 1937.
26. Lauber: Klinische und anatomische Untersuchungen ueber Drusen im Sehnervenkopf. Arch. f. Ophth., **105**:567-589, 1921.
27. Messinger, H. S., and Clarke, B. E.: Retinal Tumors in Tuberous Sclerosis; Review of the Literature and Report of a Case with Special Attention to Microscopic Structure. Arch. Ophth., **18**:1-11, 1937.
28. Nitsch, M.: Augenhintergrundsbefund bei tuberose Hirnsklerose. Zeit. f. Augenheilk., **62**:73, 1927.
29. Orzechowski, K., and Novicki, W.: Zur Pathogenese und pathologischen Anatomie der multiplen Neurofibromatose und der Sclerosis tuberosa (Neurofibromatosis universalis). Ztschr. f. d. ges. Neurol. u. Psychiat., **11**:237, 1912.
30. Pringle, J. J.: A case of congenital adenoma sebaceum. Brit. J. Dermatol., **2**:1-14, 1890.
31. Von Recklinghausen, V.: Verhandl. Berl. Gesell. f. Geburtshuelfe. 1863, 15: 73. Ein Fall von Multipler Verhaertung des Grosshirns nebst histologisch eigenartigen harten Geschwuelsten der Seitenventrikel (Glioma gangliocellulare) bei einem Neugeborenen. Arch. f. Psychiat., **11**:117-131, 1881.
32. Reese, A. B.: Relation of drusen of the optic nerve to tuberous sclerosis. Arch. Ophth., **24**:187-205, 1940.
33. Schuster, P.: Die Beziehungen der sogenannten tuberosen Sklerose des Gehirnes zur Dermatologie. Dermat. Wchnschr., **57**:1475, 1913.
34. Schuster, P.: Beitrage zur Klinik der tuberosen Sklerose der Gehirns. Deutsche Ztschr. Nervenh., **50**:96, 1914.
35. de Schweinitz, G. E.: Hyaline bodies (drusen) in the nervehead. Tr. Am. Ophth. Soc., **6**:349-359, 1891.
36. Seidel, E.: Ueber eine, sehr seltene Netzhauterkrankung als Teilerscheinung einer Allgemeinerkrankung auf ererbter Grundlage. Arch. f. Ophth., **139**:520-525, 1938.
37. Vogt, H.: Zur Diagnostik der tuberosen Sklerose. Ztschr. f. jugendl. Schwachsinn, 1907, no. 2, p. 1.
38. ———: Zur Pathologie und pathologischen Anatomie der verschiedenen Idiotieformen. Monatsschr. Psychiat. u. Neurol., 1908, **24**:106-150, 1908.
39. White, J. P., and Loewenstein, A.: An unpigmented primary tumor of the optic disc (a contribution to the knowledge of phakomata of the eye. Brit. J. Ophth., **30**:253-260, 1946.
40. Yakovlev, P. I., and Corwin, W.: A roentgenographic sign in cases of tuberous sclerosis of the brain (multiple brain-stones). Arch. Neurol. & Psychiat., **42**:1030-1037, 1939.
41. Ley, A.: La sclérose tubéreuse des circonvolutions cérébrales (maladie de Bourneville). J. belge neurol. et psychiat., **33**:679-683, 1933.
42. ———: Sclérose tubéreuse de Bourneville sans troubles mentaux avec hérédité similaire dans la descendance. J. belge neurol. et psychiat., **33**:684-687, 1933.
43. Scarpatetti: Zwei Faelle fruhezitiger Erkrankung des Zentralnervensystems. (a) Multiple tuberose Sklerose des Gehirns. Arch. f. Psychiat., **30**:537, 1898.
44. Alzheimer: Die Gruppierung der Epilepsie. Allg. Zellforsch. Psychiat., 1907.
45. Bouwdijk-Bastiaanse: Eine familiaere Form tuberose Sklerose. Nederl. Tijdsch. Geneesk., **66**:248, 1922.
46. Marcus, H., cited by Dalsgaard-Nielsen, T.: Tuberøis sklerose med. sjaeldent røntgenfund. Nord. med. tidskr., **10**:1541, 1935.
47. Berg & Vejens: Maladie kystique du poumon et sclerose tubereuse du cerveau. Acta paediat., **26**:16-30, 1939.
48. Lichtwitz, L.: Functional Pathology. New York, Greene, 1941.
49. Nieuwenhuys: Zur Kenntniss der tuberosen Hirnsklerose. Ztschr. Neurol., **24**:53.
50. Batchelor, T. M., and Maun, M. E.: Congenital glycogenic tumors of the heart. Arch. Path., **39**:67-73, 1945.

## VITREOUS HEMORRHAGE ABSORPTION\*

EXPERIMENTAL STUDY ON RABBIT EYES OF THE EFFECTS OF INTRAVITREAL HYALURONIDASE AND STREPTOKINASE-STREPTODORNASE AND ON THE INFLUENCE OF ACTH AND CORTISONE

R. A. SCHIMEK, M.D., AND E. H. STEFFENSEN, M.D.

*Detroit, Michigan*

The management of vitreous hemorrhage always has been an irksome problem for the ophthalmologist. The difficulties in estimating clinically the actual amount of blood in the vitreous and the variable absorption make clinical evaluation of therapy unreliable. This present report gives the results of an experimental study on rabbit eyes of (1) the effects of intravitreal injection of hyaluronidase and of streptokinase-streptodornase on liquefaction of the vitreous, and (2) the influence of parenteral injections of ACTH on absorption of measured amounts of autogenous blood injected into the vitreous.

### STRUCTURE OF THE VITREOUS

The vitreous resembles a true gel, holding a large quantity of water molecules in a viscous, elastic, semisolid state. In classifying constituents of the vitreous, aqueous humor solutes and metabolites (which percolate back into the vitreous) can be grouped together. Polymers of hyaluronic acid give viscosity to the vitreous<sup>1</sup> and, with the residual (insoluble) protein fraction, impart gel-like properties.

The exact physical structure of the vitreous is debated as being a gel (1) without any microscopic fibrous structure, (2) with a microscopic fibrous structure, or (3) with a framework of ultramicroscopic parallel

fibrillar sheets. Certain studies with the ordinary microscope,<sup>2</sup> dark field microscope,<sup>3, 4</sup> phase-contrast microscope,<sup>5</sup> and ultramicroscope,<sup>2, 6, 7</sup> have reported no fibers of microscopic size in fresh vitreous and only artefacts in standing vitreous or fixed vitreous specimens. Contrariwise, other similar studies<sup>2, 8-10</sup> have demonstrated microscopic fibers in fresh vitreous from various species. Furthermore coarse microscopic fibers which can be liquefied by trypsin have been demonstrated in the base of the vitreous and fine microscopic fibers which can be liquefied by collagenase have been demonstrated throughout the vitreous body.<sup>10</sup> Future evaluations must determine whether these "microscopic vitreous fibers" are real, artefact, or merely zonules which were inadvertently included in the preparation.

The concept of a structural framework in the vitreous is supported by Pirie's discovery of collagen in the residual protein fraction,<sup>11</sup> and Friedenwald's study<sup>7</sup> showing the residual protein framework to be more dense peripherally than centrally. With the electron microscope, three kinds of fibrils have been found in the vitreous: collagen fibrils, collagenlike fibrils, and fibrils of another unidentified type.<sup>8, 12, 13</sup> It should be emphasized that these fibrils identified with the electron microscope are only 1/150 the size of the controversial vitreous fibers of microscopic size.

It seems reasonable that these fibrils are arranged in the form of the parallel sheets that have been demonstrated with the ultramicroscope by Friedenwald.<sup>7</sup> These fibrillar sheets are separated by molecules of water, aqueous humor solutes, and polymerized hyaluronic acid. The hyaloid membrane can

\* From the Department of Ophthalmology of the Henry Ford Hospital. A portion of the experimental studies was carried out in the laboratories of Dr. Jack S. Guyton at the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital, and the remainder in laboratories of the Henry Ford Hospital. Some of the histologic sections were prepared by the Kresge Eye Institute. Read at the meeting of the Wilmer Resident Association in Baltimore, Maryland, April 2, 1954.



be considered a condensation of these sheets rather than a distinct membrane.

If the vitreous were merely a simple gel, the low concentration of residual protein (25 mg. percent) would not give much tensile strength. However, in the form of fibrils arranged into a framework of thin parallel ultramicroscopic sheets, this small amount of residual protein imparts the great tensile elasticity<sup>7</sup> which is characteristic of actual vitreous.

#### ABSORPTION OF VITREOUS HEMORRHAGE

In a vitreous hemorrhage, blood and debris migrate from the body of the vitreous toward the posterior pole. This is because the circulation of fluid in the vitreous is from the ciliary area to the posterior pole. Various studies<sup>14</sup> have indicated that macrophages play only a minor role in this migration. When the blood and debris reach the retinal vessels, the soluble derivatives are absorbed and the insoluble particles are phagocytosed and carried out along the perivascular spaces.

One would expect to speed blood absorption by (1) facilitating the passage of blood through the vitreous to the chorioretinal vessels, (2) increasing the capillary permeability of these vessels, and (3) stimulating phagocytosis. The effect of ACTH on the last two factors will be described later. Regarding the first factor, if the vitreous is liquefied, the blood can pass more quickly to the posterior pole for absorption.

The vitreous can be liquefied by (1) rendering soluble the normally insoluble protein framework (as by collagenase<sup>10,11</sup>), and (2) depolymerizing hyaluronic acid by hyaluronidase, which lowers the viscosity of the intralamellar fluid and permits collapse of the protein framework. Also, Pirie has shown that the stability of the protein framework is reduced when hyaluronidase depolymerizes hyaluronic acid.<sup>12</sup>

#### EFFECT OF INTRAVITREAL HYALURONIDASE

Using intravitreal injections of a hyalu-

ronidase preparation made by Karl Meyer, von Sallman reported<sup>16</sup> that (1) 100 depolymerizing units would liquefy the vitreous in rabbits and cause severe inflammatory damage, (2) one fourth of this dose still produced inflammation, and (3) experimental vitreous hemorrhage cleared faster with intravitreal hyaluronidase even if the enzyme was inactivated, suggesting that toxic impurities caused increased inflammatory reaction and phagocytosis and thus increased blood absorption. It seems logical that hyaluronidase without toxic impurities would also speed blood absorption by liquefying the vitreous.

The commercial hyaluronidase now prepared by Wyeth is apparently purer than the original preparation used by von Sallmann. The intravitreal toxicity of Wyeth hyaluronidase\* was tested in the following experiments:

#### TECHNIQUE

Using a tuberculin syringe and a fine-bore needle, injections were made behind the equator of a rabbit eye into the vitreous center under ophthalmoscopic control. Saline controls and various doses of hyaluronidase were used. The eyes were examined daily for 14 days with ophthalmoscope and slit-lamp. On the 15th day, the eyes were enucleated. By making an equatorial incision, the fluidity of the vitreous was grossly determined. Histologic examinations were obtained on all eyes.

#### RESULTS

Effects of these injections of hyaluronidase into the vitreous are shown in Table 1.

With saline (control) injections or with hyaluronidase injections below 75 turbidity-reducing units, there was no clinical or histologic evidence of inflammation; also, there was no apparent liquefaction of the vitreous. With 75 turbidity-reducing units, there was a weakly positive ray for a few days and,

\* Hyaluronidase (Wydase®) was supplied through the courtesy of Wyeth, Inc.



TABLE 1  
EFFECT OF INTRAVITREAL HYALURONIDASE

Dose TR u	Conc. u/cc.	Vol. Inj.	Inflammatory Reaction of					Vitreous Fluid	No. of Eyes
			Conj.	Aqueous Ray	Lens	Fundus	Histologic Section		
000	000	.2	-	-	-	-	-	No	3
8	150	.05	-	-	-	-	-	No	1
30	150	.2	+/-	-	-	-	-	No	1
38	1,500	.025	+/-	-	-	-	-	No	1
75	1,500	.05	+/-	+/-	-	-	+/-	No	1
150	1,500	.1	+/-	+/-	-	-	+	Yes	1
150	3,000	.05	+	+	-	+/-	+	Yes	2
300	3,000	.1	+	+	+/-	+/-	++	Yes	2
375	3,000	.125	+	+	+	++	++	Yes	1
450	3,000	.15	+	+	+	+/-	+++	Yes	1
450	6,000	.075	+	++	+	+++	++	Yes	1
750	6,000	.125	++	+	+	+++	++	Yes	1
900	6,000	.15	++	++	-	++++	++++	Yes	1

The effect of specific doses (given in total turbidity reducing units, concentration of turbidity reducing units per cc., and the volume injected) of intravitreal hyaluronidase in producing (1) liquefaction of the vitreous and (2) changes in conjunctival injection, aqueous ray, lens, ophthalmoscopic fundus picture, and histologic section.

on histologic examination, a few inflammatory cells in the posterior segment; still, there was no gross liquefaction of the vitreous. With 150 turbidity-reducing units or more, the vitreous was liquified so as to appear almost completely fluid, as contrasted to its usual gel-like viscous form.

The three eyes receiving exactly 150 turbidity-reducing units showed a positive ray for a few days, and one of the eyes had some transient slight blurring of fundus details. Otherwise, there was no evidence of clinical inflammatory reaction, with fundus details remaining clear.

Histologically, there were occasional inflammatory cells in the retina and choroid and a fair number of eosinophils and polymorphonuclear leukocytes in the ciliary body. With 300 turbidity-reducing units there was a persisting one-plus aqueous ray, transient blurring of fundus details, and on section a slightly more marked inflammatory cell infiltration of the posterior segment. With doses over 300 turbidity-reducing units, the aqueous ray became more strongly positive, with some swelling of the iris, posterior lens changes, clouding of fundus details, and his-

tologically a marked inflammatory cell infiltration of the posterior segment. With higher doses, there was some retinal necrosis.

Thus, there is a small dosage range of commercial hyaluronidase which will liquefy the vitreous of rabbit eyes and produce only minimal inflammatory changes. It is possible that liquefaction of the vitreous might be of benefit in vitreous hemorrhage and other conditions. However, the range of safety is too small to recommend any clinical use of intravitreal hyaluronidase at present.

Although Wyeth hyaluronidase appears less toxic than previous preparations, there is still enough inflammatory action to obscure the pure role of enzymatic action in clearing vitreous hemorrhage, as was true in von Sallmann's study. Therefore, further studies of the action of hyaluronidase on vitreous hemorrhage absorption have been postponed until an even purer enzyme is obtained.

#### EFFECT OF INTRAVITREAL STREPTOKINASE-STREPTODORNASE

The same technique and routine of observation were used for intravitreal injection.

tions of streptokinase-streptodornase into rabbit eyes. Table 2 shows that a concentration sufficient to liquefy the vitreous caused (ophthalmoscopic) marked clouding of fundus details, with (histologic) tremendous inflammatory-cell infiltrations of the choroid and retina with some retinal necrosis.

#### INFLUENCE OF ACTH AND CORTISONE ON ABSORPTION OF VITREOUS HEMORRHAGE

The general clinical experience with ACTH or cortisone therapy for vitreous hemorrhage has been that "no consistent therapeutic results have as yet been demonstrated."<sup>17</sup> Some hemorrhagic conditions in the vitreous have been noted to clear rapidly with small doses of ACTH,<sup>18</sup> but no accurate clinical evaluation is possible with such a variable condition without controls.

Experimental studies are also contradictory. Subconjunctival cortisone inhibits absorption of hyphema in rabbit eyes,<sup>19</sup> and parenteral cortisone inhibits blood absorption and inflammatory reaction to blood in other parts of the body of the rabbit.<sup>20</sup> It is surprising, then, that cortisone has been reported to cause increased phagocytosis and absorption of washed red blood cells from the vitreous body of the rat.<sup>21</sup> This prompted the following study on the influence of ACTH and cortisone on absorption of experimentally produced vitreous hemorrhage in rabbit eyes.

TABLE 2  
EFFECT OF INTRAVITREAL STREPTOKINASE  
AND STREPTODORNASE

Dose	No. of Rabbits	Fundus Reaction	Vitreous Fluid	Histologic Reaction
500	1	+	No	+
1,000	1	++	No	+
10,000	2	+++	Yes	++++
20,000	1	++++	Yes	++++
10,000*	2	++++	Yes	++++

The effect of specific doses of intravitreal streptokinase-streptodornase in producing liquefaction of vitreous and inflammatory changes.

\* Given with 7.5 u Wydase

#### TECHNIQUE

Using a tuberculin syringe and a small-gauge needle, blood was obtained from an ear vein of each rabbit and immediately injected posteriorly into the vitreous center. Fresh whole blood from each rabbit was used rather than washed red blood cells, to simulate more closely an actual vitreous hemorrhage. Each right eye was injected with 0.05 cc. of blood and each left eye with 0.2 cc. of blood. A standard technique observing strict sterility was used.

There were 15 control animals or 30 control eyes in this series. Sixteen rabbits or 32 eyes were treated with ACTH or cortisone. In the initial stages of the experiment, three rabbits which were treated with intramuscular cortisone (6.0 mg./kg./day) lost weight and died in about four weeks. Thereafter, subcutaneous ACTH gel (7.0 u./kg./day) was used. The ACTH animals lived throughout the experiment.

The eyes were examined with ophthalmoscope and slitlamp daily for one month and then every third day for the next six months, or until complete clearing had occurred.

#### RESULTS

The ophthalmoscopic stages of diffusion and clearing of experimental vitreous hemorrhage are recorded in Table 3. Although considerable variation existed in the rate of vitreous clearing among rabbit eyes receiving the same treatment, it was apparent that ACTH delayed the clearing of blood from the vitreous. The average number of days required for the rabbits in each group to reach the same ophthalmoscopic stage was computed and listed in Table 3. Figure 1 shows graphically how ACTH delays all stages of clearing of the vitreous hemorrhage in the eyes injected with 0.05 cc. of blood.

It is also interesting that after injection, the vitreous clouded more quickly in the control eyes (fig. 1). It was suspected that this might be due to the more rapid influx of in-

TABLE 3  
VITREOUS HEMORRHAGE ABSORPTION  
(Average rate in days)

Stage of Absorption	0.05 cc. Blood		0.2 cc. Blood	
	Control	ACTH	Control	ACTH
Initial blurring of all details	7	11	4	5
Red reflex only	9	13	5	5
Broken red reflex	10	16	10	10
Return of red reflex	32	34	35	40
Return of some blurred details	44	65	45	81
Relatively clear details	59	90	62	90
Traces of blood	76	116	78	122
No Trace	130	over 150	150	over 150

This table lists the average number of days required to reach the following ophthalmoscopic stages of vitreous hemorrhage absorption (comparing rabbit eyes with and without ACTH therapy): (1) Diffusion of injected blood with initial blurring of all fundus details, (2) red reflex only (diffusion of injected blood with all fundus details gone), (3) broken red reflex (with some dark reflex present), (4) return of red reflex (no dark reflex present), (5) return of blurred fundus details in a portion of the fundus, (6) return of relatively clear fundus details in a portion of the fundus, (7) only traces of blood remaining and, (8) no traces of blood remaining.

flammatory cells into the vitreous of the control eyes, since ACTH and cortisone suppress inflammatory reaction. To investigate this, an ACTH and a control animal were killed eight days after injection.

Using multiple histologic celloidin sections, the average macrophage and total white-cell count in the vitreous per section were determined. The results (table 4) indicated a significantly greater initial influx of white blood cells into the control eyes. These white cells were mostly macrophages and round cells. The macrophages were fre-

quently swollen with ingested red cells and debris, and they were often clumped together on histologic sections, these clumps apparently corresponding to rather large vitreous floaters that could be seen with the ophthalmoscope (fig. 2).

Whitish clouds of fibrin in the vitreous were occasionally noted, and these invariably cleared with time. There may have been less fibrin formation in the ACTH group. If so, this was not of significant extent.<sup>22</sup>

TABLE 4

## WHITE BLOOD CELLS IN VITREOUS—EIGHTH DAY

Blood Injected	Rx	Average no. per Histologic Section of	
		Macrophages	Total WBC
0.05 cc.	Control	40	117
	ACTH	17	42
0.2 cc.	Control	101	198
	ACTH	23	92

The eyes of a control and an ACTH-treated rabbit were enucleated eight days after injection. From multiple celloidin sections of each eye, the average macrophage and white blood-cell count per section was made for each eye. The invasion of macrophages and WBC was suppressed with ACTH.

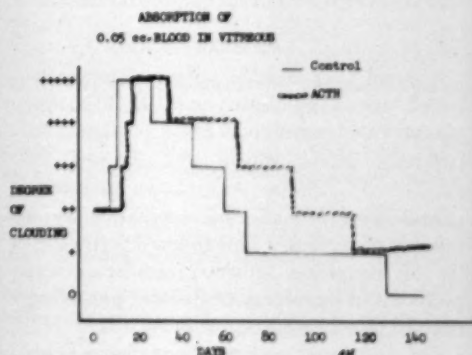


Fig. 1 (Schimek and Steffensen). This graph compares the rates of absorption of 0.05 cc. of blood from the vitreous of rabbits with and without ACTH therapy (taken from table 3).

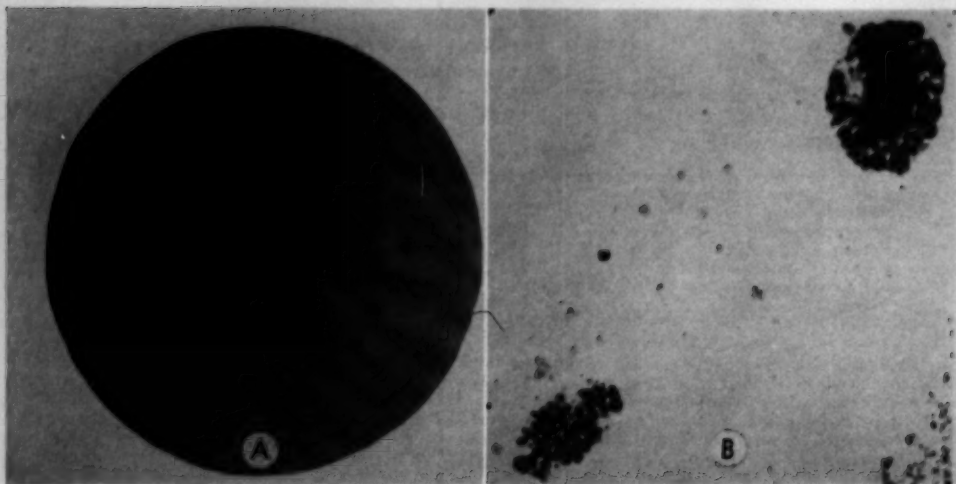


Fig. 2 (Schimek and Steffensen). (A) Fundus photograph ( $\times 16$ ) of experimental vitreous hemorrhage in a rabbit eye. Against a background of gradually clearing fundus details, discrete particles in the vitreous are visible with the ophthalmoscope. These are composed of macrophages sticking together in clumps. (B) Photomicrograph ( $\times 140$ ) of experimental vitreous hemorrhage in a rabbit eye. Macrophages which have phagocytosed red cells and debris are sticking together in clumps.

Seven months after injection (or after complete clearing), histologic sections were obtained on all eyes. Two eyes treated with ACTH showed formation of connective tissue in the vitreous. In one of the cases, this connective tissue clearly originated from the scleral puncture wound. Otherwise, there was no evidence of retinitis proliferans.

#### COMMENT

Control eyes usually appeared more injected than eyes treated with ACTH. Apparently the intravitreal blood produced an irritating effect which was blocked by ACTH. ACTH has been shown to reduce permeability of inflamed capillaries by a number of studies.<sup>23</sup> This reduced permeability of somewhat inflamed capillaries was probably an important mechanism producing delayed blood absorption with ACTH.

On histologic section, hemoglobin-laden macrophages could be seen passing into the

retina and circulation. Since ACTH was found to inhibit invasion of macrophages, this would delay clearing of the vitreous hemorrhage. Another possible factor is that ACTH may produce a diminution of the hyaluronidase content of the aqueous.<sup>24</sup>

#### SUMMARY

1. Intravitreal injection of 150 units of hyaluronidase liquefied the vitreous in rabbit eyes with only mild inflammatory reaction. Larger doses caused marked inflammation, and some retinal necrosis, while smaller doses did not liquefy the vitreous.

2. Intravitreal injection of streptokinase-streptodornase did not liquefy vitreous except in doses producing necrosis and marked inflammation.

3. Systemic injections of ACTH slowed the absorption of blood from the vitreous of rabbit eyes.

*Henry Ford Hospital (2).*

#### REFERENCES

1. Meyer, K., and Palmer, J. W.: On glycoproteins: II. The polysaccharides of vitreous humor and umbilical cord. *J. Biol. Chem.*, 114:689-703 (July) 1936.

2. Duke-Elder, W. S.: The nature of the vitreous body. *Brit. J. Ophthalm.*, Supp. 4, 1930.
3. Cattaneo, D.: Osservazioni sulla struttura del vitreo. *Atti d. r. Accad. naz. d. Lincei*, **12**:599-604, 1930.
4. Bruni, A. C.: *Arch. ital. anat. e. embriol.*, **49**:229, 1943 (Cited by Rossi<sup>5</sup>).
5. Rossi, A. A.: Structure of the vitreous body-observations by means of the phase-contrast microscope. *Brit. J. of Ophthalm.*, **37**:343, 1953.
- 6a. Baurmann, M.: *Arch. f. Ophthalm.*, **111**:352, 1923; **114**:276, 1924; **117**:304, 1926 (Cited by Grignolo<sup>8</sup>).
- 6b. Heesch, K.: *Klin. Monatsbl. f. Augenh.*, **77**:601, 1926; *Arch. Augenh.*, **98**:129, 1927 (Cited by Grignolo<sup>8</sup>).
- 6c. Stroemberg: Cited by Lauber, H.: In von Möllendorf, W.: *Handbuch der mikroskopischen Anatomie des Menschen*, Berlin, Julius Springer, 1936, v. 3, Pt. 2, p. 497.
7. Friedenwald, J., and Stiehler, P.: Structure of the vitreous. *Arch. Ophthalm.*, **14**:789 (Nov.) 1935.
8. Grignolo, A.: Fibrous components of the vitreous body. *Arch. Ophthalm.*, **47**:760-774, 1952.
9. Schwarz, W., and Schuchardt, E.: Struktur des frischen glaskörpers; Untersuchungen in phasenkontrast-, dunkelfeld, und immersions-ultra-mikroskop. *Ztschr. Zellforsch.*, **35**:293-310, 1950.
10. Bembridge, B. A., Crawford, G. N. C., and Pirie, A.: Phase-contrast microscopy of the animal vitreous body. *Brit. J. Ophthalm.*, **36**:131-142, 1952.
11. Pirie, A., Schmidt, G., and Waters, J. W.: Ox vitreous humor: 1. The residual protein. *Brit. J. Ophthalm.*, **32**:321, 1948.
12. Schwarz, W.: Elektronenmikroskopische Untersuchungen über die Glaskörperstrukturen im Rinderauge. *Ztschr. Zellforsch.*, **36**:45-61, 1951.
13. Matoltsy, A. G., Gross, J., and Grignolo, A.: A study of the fibrous components of the vitreous body by the electron microscope. *Proc. Soc. Exper. Biol. & Med.*, **76**:857 (Apr.) 1951.
- 14a. Fuchs, E.: Zur pathologischen Anatomie der Glaskörperblutungen. *Arch. f. Ophthalm.*, **99**:202-248, 1919.
- 14b. Oguchi, C.: Ueber die Wirkung von Blutinjektionen in den Glaskörper nebst Bemerkungen uver die sog. Retinitis proliferans. *Arch. f. Ophthalm.*, **84**:446-520, 1913.
- 14c. Kiriya, G.: Experimentelle Untersuchungen uver die Resorptionmechanismen in der Klaskörperblutung und die Beförderungsmittel der Resorption derselben beim Kaninchen. *Zentralbl. f. d. ges. Ophthalm.*, **42**:469, 1938-39.
- 15a. Pirie, A.: Hyaluronic acid in ox vitreous. *Brit. J. Ophthalm.*, **33**:281, 1949.
- 15b. ———: Effect of hyaluronidase injection on vitreous humor of rabbit. *Brit. J. Ophthalm.*, **33**:678-684 (Nov.) 1949.
- 16a. von Sallmann, L.: Experimental studies on the vitreous: I. Experiments on diffusion in the vitreous and on permeability of its surface condensation layer. *Arch. Ophthalm.*, **42**:583-595 (Nov.) 1949.
- 16b. ———: Experimental studies on the vitreous: II. Experiments on disappearance of red blood cells from the vitreous. *Arch. Ophthalm.*, **43**:638-653 (Apr.) 1950.
17. Woods, A. C.: Uses and limitations of ACTH and cortisone in ophthalmology. *Brit. J. Ophthalm.*, **36**:401, 1952.
18. Steffensen, E. H.: Unpublished data.
19. Benedict, W. H., and Hollenhorst, R. W.: Cortisone and blood absorption. *Am. J. Ophthalm.*, **36**:247 (Feb.) 1953.
20. Blunt, J. W., Plotz, C. M., Lattes, R., Howes, E. L., Meyer, K., and Ragan, C.: Effect of cortisone on experimental fractures in the rabbit. *Proc. Soc. Exper. Biol. & Med.*, **73**:678-681 (Apr.) 1950.
21. von Sallmann, L., Jones, I. S., Wiggins, R. L., and Locke, B. D.: The influence of cortisone on wound healing, macrophagocytosis, and capillary permeability. *Wien. klin. Wchnschr.*, **63**:684-686, 1951.
22. Magni, S.: Anti-exudative and fibrinolytic action of cortisone in eye diseases. *Boll. d'ocul.*, **31**:147-156 (Mar.) 1952.
- 23a. Armstrong, S. H., and Irons, E. N.: Physiological considerations of ACTH and cortisone therapy with reference to ophthalmology. *Arch. Ophthalm.*, **45**:251, 1951.
- 23b. Cook, C. A. G., and MacDonald, R. K.: Effect of cortisone on the permeability of the blood aqueous barrier to fluorescein. *Brit. J. Ophthalm.*, **35**:730, 1951.
- 23c. Menkin, V.: Localization of cortisone in an inflamed area. *Federation Proc.*, **11**:106, 1952.
- 23d. Soskin, S.: Physiologic basis for therapeutic effects of cortisone. *Rev. Gastroenterol.*, **19**:808-816, 1952.
- 23e. Woods, A. C., and Wood, R. M.: The action of ACTH and cortisone on experimental ocular inflammation. *Bull. Johns Hopkins Hosp.*, **87**:482, 1950.
- 23f. Harris, J. E.: Pharmacology and toxicology. *Arch. Ophthalm.*, **50**:192 (Aug.) 1953.
24. Lepri and Monanari: The effect of the corticotrophic hormone (ACTH), desoxycorticosterone, and adrenal cortex extract on the hyaluronidase content of the aqueous. *Arch. ottal.*, **55**:329-340 (May-June) 1951.



## MECHANISM OF MIOPIESIN FORMATION\*

ERNST SCHMERL,<sup>†</sup> M.D., ALBERT A. DIETZ, Ph.D.,  
AND BERNHARD STEINBERG, M.D.

Toledo, Ohio

Previous articles outlined the role of the neurovascular mechanism in maintaining intraocular pressure. Investigations reported in other papers indicated that the pituitary gland elaborated two hormones.<sup>1</sup> One of them, hyperpiesin, increased intraocular pressure. The other, miopiesin, decreased it. Multiple doses of miopiesin produced a marked decrease in tension, and larger quantities of hyperpiesin resulted in a considerable increase. When a critical point of tension was reached, signs of acute glaucoma appeared.<sup>2</sup>

Hyperpiesin acts on the parasympathetic centers and then by way of the ciliary ganglion, resulting in production of vascular dilatation in the eye and an increase in tension.<sup>3</sup> Miopiesin, on the other hand, activates the sympathetic centers and then the superior cervical ganglion, with a resultant vascular contraction in the eye and a decrease in tension.<sup>3</sup>

Spinal fluid was found to contain both hormones in quantities which produced a physiologic balance under normal conditions.<sup>1</sup> Exposure of animals to intense light or to darkness disturbed this physiologic balance. Rabbits, which are nocturnal animals, showed the appearance of excess of hyperpiesin when subjected to light. Darkness induced a demonstrable increase of miopiesin.<sup>3</sup> The reverse was true in man.

Other experiments suggested an additional method for demonstrating physiologic equilibrium and the presence of either miopiesin or hyperpiesin. Extirpation of the superior cervical ganglion removed the sym-

pathetic conveyor. This procedure blocked the action of miopiesin.

The only stimuli which remain effective are those which pass along the parasympathetic system and produce an increase in tension.<sup>3</sup> By the use of animals with extirpated superior cervical ganglia, one could determine the presence of hyperpiesin in an unknown material. This method was used repeatedly in this article.

A number of experiments during the last few years indicated that the original concept of the pituitary tissue secreting miopiesin and hyperpiesin was not as simple as the former experiments appeared to indicate.<sup>4</sup> It was postulated previously that the two hormones are secreted by the posterior lobe of the pituitary gland. Previous studies showed that crude water extracts of anterior pituitary tissue, obtained from light- and dark-exposed rabbits, contained hyperpiesin.<sup>1</sup> On the other hand, extracts of posterior pituitary tissue varied in their effect upon tension, depending upon the exposure of rabbits either to light or to darkness. Further experiments involving rabbits with congenital glaucoma (buphthalmos) showed partial or complete failure of secretion of miopiesin.<sup>5</sup> Offspring of rabbits with congenital glaucoma failed to elaborate either of the two hormones.<sup>3</sup>

These various observations prompted a further study of the mechanism responsible for the production of hyperpiesin and miopiesin. An hypothesis could be drawn on the basis of the observations just recorded. Hyperpiesin is secreted by the anterior pituitary tissue. The posterior pituitary stores hyperpiesin and transforms it by some mechanism into miopiesin whenever the organism requires the hormone. The present

\* From the Toledo Hospital Institute of Medical Research. This work was supported by a grant from the Walter Snyder Ophthalmic Foundation.

<sup>†</sup> Research ophthalmologist of the Walter Snyder Ophthalmic Foundation.

study is concerned with experiments testing the validity of this concept.

#### MATERIALS AND METHODS

Rabbits were used as testing animals. They were handled repeatedly by the same individual. Intraocular pressure was determined with the Schiøtz tonometer many times on the same animals prior to the experiments. The eyes were anesthetized with a few drops of one-percent. butyn.

Spinal fluid was obtained from rabbits after they were exposed to strong light consisting of four hours of bright daylight and a 300-watt bulb placed 50 cm. from the cage. The quantity of hyperpiesin became slightly increased in the spinal fluid under these conditions.<sup>3</sup>

Posterior pituitary tissue was separated from the whole pituitary glands which were removed from rabbits exposed to normal light. The posterior pituitary tissue was ground and mixed with the spinal fluid. The mixture was drawn up into small syringes. The tips of the needles were closed with rubber stoppers.

Most of the mixtures so prepared were incubated in strong light for 70 minutes at 37°C. in a water bath in an incubator. A few mixtures were incubated in a dark incubator. Ground lens tissue in two-mg. quantities was added to some of the mixtures of posterior pituitary and spinal fluid. Posterior pituitary tissue was also homogenized with physiologic salt solution and treated in a similar manner. Spinal fluid alone was subjected to the same procedure. The latter two materials were used as controls.

After incubation, the materials were injected subcutaneously into test rabbits in quantities of 0.6 to 1.0 ml. The intraocular pressure was determined prior to and for a period of one or more hours after the injections of the several mixtures. Anterior pituitary tissue was homogenized with spinal fluid, incubated, and injected under similar conditions.

The superior cervical ganglion was re-

moved from some of the test rabbits. Absence of the ganglion allowed the recognition of hyperpiesin in materials under study. Rabbits were injected with incubated mixtures of spinal fluid and posterior pituitary tissue removed from rabbits with congenital glaucoma, posterior and anterior pituitary, and anterior pituitary with physiologic salt solution.

Franceschetti and Schläppli<sup>6</sup> injected Pitressin and obtained a decrease of intraocular pressure by 7.0 to 10 mm. Hg, along with pupillary contraction. These investigators ascribed the changes to the pressor principle in Pitressin. Evidence was presented in a previous report<sup>7</sup> that two distinct and separate centers are present for pupillary motility and for intraocular pressure. Other work in this laboratory (unpublished) indicated that neither hyperpiesin nor miopiesin is identical with the known substance in Pitressin.

To test the mechanism of hormone formation and to evaluate the presence in Pitressin of the hormones acting on intraocular pressure, batches of Pitressin were prepared in a manner similar to that used for pituitary tissue. Cysteine was added to one batch of Pitressin and incubated. All Pitressin preparations were injected subcutaneously.

Posterior pituitary tissue was subjected to dialysis. The tissue was combined with two ml. of water and the mixture was dialyzed at 3°C. against two changes of two liters each of distilled water. The total dialysis time was approximately 20 hours. Normal spinal fluid was added to the dialyzed residue of posterior pituitary tissue. The mixture was incubated and injected subcutaneously into test rabbits.

Pitressin in one-ml. volume containing 20 units of pressor substance was diluted to four ml. and dialyzed by the method described. The residue was injected into test rabbits.

#### RESULTS

Incubated spinal fluid and posterior pitui-

TABLE 1  
CONVERSION OF HYPERPIESIN TO MIOPIESIN BY A CATALYST CONTAINED IN  
THE POSTERIOR PITUITARY TISSUE

(Rabbit or human spinal fluid was incubated with posterior pituitary tissue and injected into rabbits. The effect on intraocular pressure was obtained. Changes in tension are expressed in mm. Hg [Schiotz]. - sign indicates a decrease in tension; + sign an increase; \* indicates readings obtained from material incubated in the presence of light.)

Ml. of Spinal Fluid Injected into Rabbits	Source of Spinal Fluid Used to Inject Rabbits. R = rabbit M = man	Spinal Fluid and Saline, Incubated and Injected into Rabbits (Control)		Spinal Fluid Incubated with Posterior Pituitary Tissue and Injected into:			
				Normal Rabbits		Rabbits with Superior Cervical Ganglion Removed	
		Eyes		Eyes		Eyes	
		R.	L.	R.	L.	R.	L.
1.0	R	+4.5	+9.0	- 5.0	- 5.5		
0.9	R			- 3.0	- 5.0		
1.0	R	+6.0	+4.0	0.0	0.0		
0.5	R	+2.0	+5.0	- 3.0	- 3.0	+4.5	+3.5
1.5	R			- 3.0	- 2.5	+9.5	+4.5
0.8	R			- 7.0	- 6.0	+4.5	+4.0
1.1	R			0.0	- 4.0		
0.6	R*			-12.0*	-12.0*		
5.0	M*			-10.0*	- 9.0*		
5.0	M*			-14.5*	-14.5*		
5.0	M*			- 8.5*	- 8.0*		

INTERPRETATION:

When posterior pituitary tissue was incubated with spinal fluid which contained hyperpiesin, a conversion took place of a portion of hyperpiesin to miopiesin. This conversion was assumed to be accomplished by a catalyst.

The superior cervical ganglion transmits impulses which contract capillaries and lower intraocular pressure. Removal of this ganglion prevents the mediation of these stimuli. This experiment indicated that conversion of hyperpiesin to miopiesin was not complete.

TABLE 2  
DEMONSTRATION OF HYPERPIESIN AND MIOPIESIN IN PITRESSIN. CONVERSION  
OF PITRESSIN HYPERPIESIN INTO MIOPIESIN

(Pitressin was incubated in the presence of light and injected into rabbits. The effect on intraocular pressure was obtained. Changes in tension are expressed in mm. Hg [Schiotz]. - sign indicates a decrease of tension; + sign indicates an increase.

Units of Pitressin Injected into the Animals	Pitressin without Incubation Injected into Normal Animals		Pitressin without Incubation Injected into Animals without Superior Cervical Ganglion		Incubated Pitressin Injected into Normal Animals	
	Eye		Eye		Eye	
	R.	L.	R.	L.	R.	L.
0.1	0.0	0.0			-4.25	-4.25
0.1	0.0	0.0			-5.00	-6.75
0.5	-1.5	-1.0	+8.00	+9.90	-4.00	-5.00
0.5	+0.7	-0.7	+5.25	+3.25	-5.75	-5.50
0.5			+9.00	+7.50	-6.00	-6.00
0.5					-5.00	-7.00
0.5					-4.00	-5.00
0.5					-4.50	-4.50

INTERPRETATION:

Under normal conditions, pitressin contains hyperpiesin and miopiesin in quantities which produce physiologic balance. Upon removal of the pathway (superior cervical ganglion) which transmits impulses resulting in reduction of tension, hyperpiesin can be demonstrated. Incubation of pitressin converts hyperpiesin into miopiesin.

TABLE 3

DETERMINATION OF PRESENCE OF THE CATALYST IN DIALYZED RESIDUE OF RABBITS' POSTERIOR PITUITARY TISSUE

(Human spinal fluid and posterior pituitary tissue were incubated alone and combined. The pituitary tissue was dialyzed and the residue was injected into normal rabbits and into those with excised superior cervical ganglion. Intraocular pressure was determined in mm. Hg [Schjötz].)

Human Spinal Fluid Injected into:				Dialyzed Residue of Posterior Pituitary Tissue Injected into:				Human Spinal Fluid and Dialyzed Posterior Pituitary Tissue Injected into:			
Normal Rabbits		Rabbits with Excised Superior Cervical Ganglion		Normal Rabbits		Rabbits with Excised Superior Cervical Ganglion		Normal Rabbits		Rabbits with Excised Superior Cervical Ganglion	
Eye		Eye		Eye		Eye		Eye		Eye	
R.	L.	R.	L.	R.	L.	R.	L.	R.	L.	R.	L.
0	-1	+6.0	+6.0	-0.75	-1.5	0	0.00	-5.25	-5.50	+3.0	+1.50
0	-2	+6.0	+5.5	-0.75	0.0	0	+0.75	-5.50	-5.25	+3.0	+3.25

## INTERPRETATION:

Human spinal fluid contains hyperpiesin and miopiesin in quantities to produce physiologic balance. When the pathway for action of miopiesin is removed (superior cervical ganglion), presence of hyperpiesin becomes apparent.

Residue of dialyzed posterior pituitary tissue which retains large protein molecules contains the catalyst which transforms hyperpiesin into miopiesin. Similar experiments with pitressin resulted in comparable findings.

tary tissue produced in a normal rabbit a decrease of tension up to 14.5 mm. Hg. Incubated spinal fluid from animals exposed to light resulted in an increase of tension up to 9.0 mm. Hg (table 1). Posterior pituitary tissue incubated alone gave no significant changes in intraocular pressure. These findings suggested the presence of some catalyst in the posterior pituitary tissue which converted hyperpiesin to miopiesin.

When the posterior pituitary tissue was dialyzed and the residue incubated with spinal fluid containing an excess of hyperpiesin, a decrease in tension up to 5.0 mm. Hg was obtained (table 3). This experiment suggested that the catalyst was a protein molecule of sufficient weight to be retained by a semipermeable membrane.

Incubated Pitressin showed presence of a similar catalyst which converted hyperpiesin into miopiesin (table 2). A decrease in tension up to 7.0 mm. Hg was obtained with incubated Pitressin.

Addition of lens substance to incubated

posterior pituitary tissue and spinal fluid showed an inhibition of the catalyst. Cysteine produced a similar inhibition when added to Pitressin.

When incubated mixtures of spinal fluid and posterior pituitary or Pitressin, prior to or after dialysis, were injected into test rabbits without superior cervical ganglia, increases of tension up to 9.0 mm. Hg were obtained (tables 1, 2, and 3). These experiments indicated that only partial conversion of hyperpiesin to miopiesin had taken place.

Injection of incubated spinal fluid with anterior pituitary tissue resulted in an increase in tension of 4.0 to 5.0 mm. Hg. This experiment indicated that anterior pituitary tissue secretes hyperpiesin but it lacks the presence of the catalyst.

To determine if rabbits with congenital glaucoma possess the catalyst, the posterior pituitary tissue of these animals was incubated with human spinal fluid and injected into test rabbits. No significant changes in tension were found. Injections of anterior pituitary from the rabbits with buphthalmos

produced an increase in tension up to 7.0 mm. Hg. Administration of incubated posterior and anterior pituitary tissue gave an increase of tension. These experiments indicated that rabbits with congenital glaucoma do not possess the catalyst which transforms hyperpiesin into miopiesin.

#### DISCUSSION AND SUMMARY

On the basis of the former studies and the experiments presented in this article, the mechanism of hyperpiesin and miopiesin formation has been clarified further. It appears that anterior pituitary tissue secretes hyperpiesin. The hormone is modified quantitatively according to the demands of the organism by the posterior pituitary tissue. Hyperpiesin is acted upon by some catalytic substance, probably an enzyme, and a part

of the hormone is converted to miopiesin. A physiologic balance is established thereby and maintained as long as normal conditions exist.

It is not unlikely that hyperpiesin is stored in the posterior pituitary tissue and conversion proceeds according to the requirements of the body in its effort to maintain an equilibrium. The catalyst does not pass through a semipermeable membrane and is activated by light and heat (37°C.). It is inhibited by lens substance and cysteine. If the catalyst is an enzyme, it may be considered as hyperpiesinase.

Rabbits with congenital glaucoma lack, apparently, this catalyst. These animals are able to secrete hyperpiesin but fail to convert it to miopiesin.

2805 Oatis Avenue (6)

#### REFERENCES

1. Schmerl, E., and Steinberg, B.: Central control of intraocular pressure by active principals. *Am. J. Ophth.*, **31**:1097-1101 (Sept.) 1948.
2. ———: Quantitative effects of miopiesin and hyperpiesin on intraocular pressure. *Am. J. Ophth.*, **39**: 547 (Apr.) 1955.
3. ———: The role of ciliary and superior cervical ganglia in ocular tension. *Am. J. Ophth.*, **32**:947-950 (July) 1949.
4. ———: The role of the diencephalon in regulating ocular tension. *Am. J. Ophth.*, **31**:155-158 (Feb.) 1948.
5. ———: The neurovascular mechanism controlling ocular tension in congenital glaucoma of rabbits. *Am. J. Ophth.*, **35**:696-701 (May) 1952.
6. Franceschetti, A., and Schläppli, V. The action of the hormones of the posterior pituitary upon pupil and ocular tension. *Deutsche med. Wchnschr.*, **66**:529-531, 1940.
7. Schmerl, E., and Steinberg, B.: Separation of diencephalic centers concerned with pupillary motility and ocular tension. *Am. J. Ophth.*, **33**:1379-1381 (Sept.) 1950.



## THE EFFECT OF THE BROAD AND MEDIUM SPECTRUM ANTIBIOTICS ON THE VIRUS OF HERPES SIMPLEX\*

RUTH G. MACKNESON, B.A., AND H. L. ORMSBY, M.D.

*Toronto, Ontario*

Braley and Sanders<sup>1</sup> (1948) were the first to report the beneficial effect of aureomycin on herpes-simplex infections of the human cornea. In support of these clinical observations, Braley and Alexander<sup>2</sup> (1949) subsequently reported *in vitro* studies in which aureomycin inhibited the strain of herpes-simplex virus used in their experiments.

Thygeson and Hogan<sup>3</sup> (1950) also reported successful treatment of human herpes-simplex infections with aureomycin. In a series of 24 patients with dendritic ulcers treated with aureomycin borate, they observed clinical cure in 14. However, Geller and Thygeson<sup>4</sup> (1951) were unable to demonstrate any beneficial effect with topical aureomycin in the treatment of herpetic keratitis in rabbits, nor were they able to find any *in vitro* inhibition of the virus with either aureomycin, chloromycetin, or terramycin.

Baldrige and Blank<sup>5</sup> (1949), using chick-embryo techniques, found that aureomycin had neither an *in vivo* nor an *in vitro* inhibitory effect on herpes-simplex virus.

Recently, a number of new broad- and medium-spectrum antibiotics have become available and are being used extensively in the treatment of external eye infections. This study was undertaken to determine the effect of aureomycin on our own strain of herpes-simplex virus which had been isolated from a human corneal ulcer, and to compare this effect with that of chloromycetin, terramycin, magnamycin, erythromycin, and puromycin. Since many of these antibiotics are in the form of salts in solution, the hydrogen-ion concentration of which differs, it was first

necessary to determine the effect of pH on the virus.

### EFFECT OF pH ON THE HERPES-SIMPLEX VIRUS

To test the effect of pH on the virus, two buffers were chosen. McIlvaine's<sup>†</sup> buffer was used from pH 2.5 to 7.0 and Sorensen's<sup>‡</sup> buffer from pH 8.5 to 11.5. The pH of all buffer solutions was determined both before and after sterilization immediately before use.

A 20-percent suspension of infected mouse brain was emulsified with four times its weight of buffered gelatin saline, containing 1,000 units of penicillin and 1,000 µg. of streptomycin per ml. The resultant mixture was centrifuged lightly to remove coarse particles and used immediately. To 0.5 cc. of this suspension, an equal volume of the desired buffer was added. This mixture was incubated at 37.5°C. for four hours, and then diluted in tenfold steps to 10<sup>-4</sup>. Five mice were inoculated with 0.03 cc. of each dilution intracerebrally. Death was the criterion of infection and those deaths occurring between 24 hours and 28 days after inoculation were considered significant. The L.D.<sub>50</sub> was determined by the Karber method and a change of titer of one log unit was considered significant.

### RESULTS

From Table 1 it will be seen that within the pH range of 4.0 to 10.0, the virus was not affected. Since the pH of the antibiotic mixtures with buffered gelatin saline

<sup>†</sup> McIlvaine's buffer: 0.2 M disodium phosphate and 0.1 M citric acid.

<sup>‡</sup> Sorensen's buffer: 7.505 gm. glycocoll plus 5.85 gm. sodium chloride per liter, buffered with 0.1 N sodium hydroxide.

\* From the Departments of Ophthalmology and Bacteriology, University of Toronto.

TABLE 1  
EFFECT OF pH ON THE TITER OF THE  
HERPES-SIMPLEX VIRUS

pH of Buffer	Resultant Titer (L.D. <sub>50</sub> )
2.5	10 <sup>-1.5</sup>
4.0	10 <sup>-2.1</sup>
5.5	10 <sup>-2.5</sup>
7.0	10 <sup>-2.5</sup>
8.5	10 <sup>-3.1</sup>
10.0	10 <sup>-3.5</sup>
11.5	10 <sup>-3.5</sup>
Buffered gelatin saline with 1,000 units penicillin and 1,000 µg. streptomycin	10 <sup>-3.5</sup>

in all subsequent experiments fell within the range of 5.0 and 9.0, no further buffering of these solutions was considered necessary.

#### EFFECT OF ANTIBIOTICS ON THE HERPES-SIMPLEX VIRUS

Infected mouse brain was prepared in the manner described for the pH studies and to this were added antibiotic solutions to reach final concentrations of two or five mg./cc. (table 2). These mixtures were incubated at 37.5° C. for four hours and then diluted in

tenfold steps to 10<sup>-4</sup>. Intracerebral inoculations of mice and L.D.<sub>50</sub> determinations were carried out as previously described.

Controls consisted of buffered gelatin saline with added penicillin (1,000 units/cc.) and streptomycin (1,000 µg./cc.) and distilled water. With aureomycin, additional controls consisting of the inactivated drug were used.

#### RESULTS

From Table 2 it may be seen that the only antibiotics used in these experiments having an inhibitory effect on the herpes-simplex virus were aureomycin and puromycin. Inactivation of aureomycin by heat destroyed its inhibitory effect on the virus.

#### DISCUSSION

This work confirms the original experiments of Braley and Alexander,<sup>2</sup> in which the herpes-simplex virus was inhibited by aureomycin borate in concentrations of 5.0 mg./cc. and 2.0 mg./cc. Although recent observers do not confirm the early reports of

TABLE 2  
IN VITRO EFFECT OF ANTIBIOTICS ON THE HERPES-SIMPLEX VIRUS

Solution	Control	Concentration	Resultant Titer (L.D. <sub>50</sub> ) Less Than
Aureomycin <sup>1</sup>	Inactivated aureomycin	5 mg./cc. 5 mg./cc.	10 <sup>-1</sup> 10 <sup>-2.5</sup>
Aureomycin	Inactivated aureomycin	2 mg./cc. 2 mg./cc.	10 <sup>-2.1</sup> 10 <sup>-3.5</sup>
Achromycin <sup>2</sup> Chloromycetin <sup>3</sup> Erythromycin <sup>4</sup> Magnamycin <sup>5</sup> hydrochloride Magnamycin <sup>5</sup> sulfate Puromycin <sup>7</sup>	Buffered saline with penicillin & streptomycin -Distilled water	2 mg./cc. 2 mg./cc. 2 mg./cc. 2 mg./cc. 2 mg./cc. 2 mg./cc.	10 <sup>-2.5</sup> 10 <sup>-3.5</sup> 10 <sup>-3.5</sup> 10 <sup>-3.5</sup> 10 <sup>-3.5</sup> 10 <sup>-3.5</sup>

<sup>1</sup> Aureomycin hydrochloride in borate solution (ophthalmic), Lot #4475-127CX2.

<sup>2</sup> Achromycin hydrochloride, Lot #5747-45.

<sup>3</sup> Chloromycetin synthetic, Lot #D126C.

<sup>4</sup> Erythromycin Lilly (Ilotycin), Lot #9853-615393.

<sup>5</sup> Magnamycin hydrochloride, Lot #539094.

<sup>6</sup> Magnamycin sulphate, Lot #17KVS28011.

<sup>7</sup> Puromycin hydrochloride, Lot #1678-B-53B.

clinical response in human herpetic infections to this antibiotic, these *in vitro* studies nevertheless suggest that aureomycin is the antibiotic of choice when one wishes to use such a drug in the treatment of herpes-simplex infections.

Although the concentrations of antibiotics used in these experiments exceed the levels usually obtained in the body fluids, they are comparable to those of ophthalmic solutions and ointments. Such concentrations of aureomycin might be expected to neutralize free virus in the conjunctival sac.

The slight inhibitory effect of puromycin on the virus would indicate its trial in human infections.

#### CONCLUSIONS

Fresh aureomycin borate at concentrations of 5.0 mg./cc. and 2.0 mg./cc. significantly

lowered the titer of herpes-simplex virus suspension.

Achromycin, chloromycetin, erythromycin, and magnamycin in concentrations of 2.0 mg./cc. had no effect on the titer of the virus suspension.

Puromycin in concentration of 2.0 mg./cc. had a slight inhibitory effect on the virus.

The strain of herpes-simplex virus used in these experiments was stable in solutions of pH 4.0 to 10.0.

*Banting Institute.*

Antibiotics used in this study were provided by Lederle Laboratories (aureomycin, achromycin, and puromycin); Parke, Davis & Co. (chloromycetin); Eli Lilly & Co. (erythromycin); and Chas. Pfizer & Co. (magnamycin). This study was carried out under the National Health Grant #605-9-63 "Ocular diseases of virus aetiology." Additional help was provided through the Snyder Foundation for Ophthalmological Research, New York.

#### REFERENCES

1. Braley, A. E., and Sanders, M.: Aureomycin in ocular infections. *J.A.M.A.*, **138**:426-427 (Oct.) 1948.
2. Braley, A. E., and Alexander, R. C.: Experimental and clinical use of aureomycin in herpes simplex. *Tr. Am. Ophth. Soc.*, **47**:335-348, 1949.
3. Thygeson, P., and Hogan, M. J.: Aureomycin in the treatment of herpes-simplex corneae. *Am. J. Ophth.*, **33**:958-960, 1950.
4. Geller, H. O., and Thygeson, P.: Aureomycin, chloromycetin, and terramycin in experimental herpes-simplex virus infections. *Am. J. Ophth.*, **34**:165, 1951.
5. Baldrige, G. D., and Blank, H.: Effect of aureomycin on herpes simplex virus in embryonated eggs. *Proc. Soc. Exper. Biol. & Med.*, **72**:560-563, 1949.

#### LABORATORY OBSERVATIONS ON THE OCULAR USE OF TETRACYCLINE\*

J. W. HALLETT, M.D., KHALIDA NAIB, M.D., AND IRVING H. LEOPOLD, M.D.  
*Philadelphia, Pennsylvania*

The chemical similarity between aureomycin (chlortetracycline) and terramycin (oxytetracycline) led to the preparation of the structure common to both of these antibiotics, namely, tetracycline.<sup>1,2</sup> This new antibiotic, like its chemical cousins, is

claimed to have the same broad-spectrum activity against gram-negative and gram-positive bacteria, certain viruses, and rickettsial infections.<sup>3</sup> Solutions in 0.85-percent sodium chloride maintained undiminished their antibacterial activity after three weeks' storage at 5°C., whereas similar preparations of chlortetracycline and oxytetracycline started deteriorating in between 24 hours and one week.<sup>4</sup> Tetracycline is said to diffuse effectively into body tissues and fluids<sup>5</sup> and to elicit very low toxicity data and a wide margin of safety.<sup>6</sup>

\*From the Research Department, Wills Eye Hospital. Presented in part at the sixth annual Wills Eye Hospital conference, February 19, 1954. We are indebted to J. B. Roerig and Company and Lederle Laboratories Division, American Cyanamid Company, for generous supplies of tetracycline hydrochloride in the forms of Tetracyn and Achromycin respectively.

No reports are available at present on the ocular effects of tetracycline. This paper deals with some laboratory observations on that aspect. The tetracycline used was provided as sterile crystals in sealed vials. Solutions were freshly prepared with sterile distilled water.

#### SENSITIVITY TESTS

Filter-paper discs, 8.0 mm. in diameter, were saturated with various concentrations of the antibiotic and placed upon the surface of blood-agar plates which just previously had been streaked heavily with actively growing 24-hour blood-agar cultures of the bacteria. The zones of inhibition of bacterial growth were measured in 24 hours. These are recorded graphically in Figure 1 which indicates the preponderance of effectivity against the gram-positive organisms.

It is noteworthy that the *Staphylococcus albus*, labelled as 1 in the graph, was found previously to be similarly resistant to chlor-

tetracycline and oxytetracycline. Such cross resistance corroborates Finland's<sup>4</sup> findings that organisms "highly resistant to any one of the agents were always resistant in about the same degree to each of the other two."

#### OCULAR PENETRATION STUDIES

##### 1. INTRAVENOUS INJECTIONS

The left eyes of normal adult rabbits were prepared with a standard corneal abrasion produced by scraping away the epithelium within a circular area, 3.5 mm. in diameter, outlined with a trephine. The right eye remained intact. In the first group of animals 50 mg. tetracycline dissolved in 1.0 cc. of water were injected intravenously.

The animals were divided into five smaller groups, the first of which was killed at the end of one hour, the second at the end of two hours, the third at four hours, the fourth at eight hours, and the fifth at 24 hours.

The concentration of tetracycline in micrograms per cc. in the heart blood, cornea,

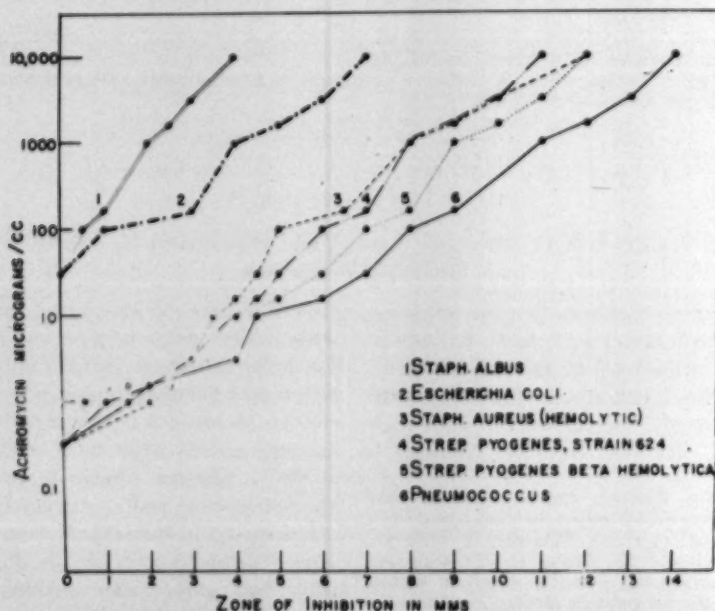


Fig. 1 (Hallett, Naib, and Leopold). Zones of inhibition of bacterial growth measured in 24 hours.

TABLE 1  
INTRAVENOUS INJECTION OF 50 MG. TETRACYCLINE  
(Concentrations in micrograms per cc.)

Time (hr.)	Intact Eye				Abraded Eye		
	Blood	Cornea	Aqueous	Vitreous	Cornea	Aqueous	Vitreous
1	5.0	0	0.0	0	0	0.0	0
2	10.0	0	0.3	0	0	0.0	0
4	10.0	0	0.2	0	0	0.2	0
8	0.3	0	0.0	0	0	0.0	0
24	0.0	0	0.0	0	0	0.0	0

aqueous, and vitreous was determined by the filter-paper disc method. They are listed in Table 1. Each figure represents the average of three animals.

The same procedure was repeated on another group of rabbits which received 100 mg. tetracycline in 1.0 cc. of water intravenously. One half of the group was killed at the end of two hours, the other half at the end of four hours. The concentrations of tetracycline are listed in Table 2; each figure represents the average of three animals.

Another group of rabbits was subjected to the same procedure but received 150 mg. tetracycline in 1.0 cc. water intravenously. One third of this group was killed at the end of one hour, another third at the end of two hours, and the final third at the end of four hours. The concentrations of tetracycline are listed in Table 3; each figure represents the average of three animals.

One may conclude that, despite adequate blood levels up to four hours, theoretically effective aqueous levels are obtained only with 100 mg. injections or higher. Corneal levels appear up to one hour with 150 mg. injections, which also produce very small

vitreous levels. A word of caution, however, should be interjected at this point; our next step was to try 200 mg. intravenous injections and all three rabbits, so injected, died within a few minutes in convulsions.

## 2. SUBCONJUNCTIVAL INJECTIONS

One eye of normal adult rabbits was prepared with a standard corneal abrasion. Bulbar subconjunctival injections of tetracycline, 10 mg./cc. in 0.5 cc. volume, were made into all eyes. Cornea, aqueous, and vitreous levels were determined in one, two and four hours. The results, listed in Table 4, are the average, in each instance, of six eyes.

Obviously very adequate corneal and aqueous levels up to four hours result from subconjunctival injections in the quantity chosen. Even quite adequate vitreous levels at the end of one hour result from this treatment. The inflamed eyes stored the antibiotic more generously than the normal eye.

## 3. CORNEAL BATH

A group of rabbits was prepared with a standard corneal abrasion of one eye. A corneal bath of tetracycline, 25 mg./cc., was applied to all eyes for five minutes. Cornea,

TABLE 2  
INTRAVENOUS INJECTION OF 100 MG. TETRACYCLINE  
(Concentrations in micrograms per cc.)

Time (hr.)	Intact Eye				Abraded Eye		
	Blood	Cornea	Aqueous	Vitreous	Cornea	Aqueous	Vitreous
2	20.0	0	1.0	0	0	1.0	0
4	1.0	0	0.0	0	0	0.0	0



TABLE 3  
INTRAVENOUS INJECTION OF 150 MG. TETRACYCLINE  
(Concentrations in micrograms per cc.)

Time (hr.)	Intact Eye				Abraded Eye		
	Blood	Cornea	Aqueous	Vitreous	Cornea	Aqueous	Vitreous
1	45.0	0.5	7.0	0.2	0.8	16.0	0.2
2	10.0	0.0	2.0	0.0	0.0	4.0	0.0
4	2.0	0.0	0.0	0.0	0.0	0.0	0.0

aqueous, and vitreous levels were determined in one, two and four hours. The results, listed in Table 5, are the average, in each instance, of six eyes.

Very effective corneal levels for four hours result from this modality. Aqueous levels are adequate up to two hours in the intact and up to four hours in the inflamed eye. No vitreous levels were noted.

#### 4. EYE DROPS

A group of rabbits was prepared with a standard corneal abrasion of one eye and then treated with drops of tetracycline solution in a concentration of 25 mg./cc. The drops were instilled upon all eyes every 10 minutes for one hour. Cornea, aqueous, and vitreous levels were determined as already described at one, two and four hours. The results, listed in Table 6 (each figure representing the average of six eyes), are roughly similar to those obtained with the corneal bath.

#### OCULAR TOLERANCE STUDIES

##### 1. SUBCONJUNCTIVAL INJECTIONS

Four normal adult rabbit eyes were chosen. Injections of 0.5 cc. volume were made under

the superior bulbar conjunctiva of each eye twice daily for three days. The first eye received a concentration of 1.0 mg./cc., the second 5.0 mg./cc., the third 10 mg./cc., and the fourth 25 mg./cc.

Twenty-four hours later the 1.0-mg. eye was clear. The 5.0-mg. eye presented slight conjunctival congestion and swelling. The 10-mg. eye developed swollen red lids and conjunctiva, secretion, and corneal haze. The 25-mg. eye showed the same picture in a more severe degree, plus sloughing of the conjunctiva and a muddy iris.

By the end of 48 hours the 1.0-mg. eye was clear and the 5.0 mg. eye showed only a slight thickened conjunctiva. The 10-mg. eye presented swollen red lids, thick conjunctiva, secretion, and corneal haze. The 25-mg. eye had more severely swollen red lids, secretion, thickened and sloughing conjunctiva, diffusely hazy cornea, and iritis.

By the end of 72 hours the 1.0- and 5.0-mg. eyes showed only slight thickening of the conjunctiva. The 10-mg. eye presented thick red lids and conjunctiva. The 25-mg. eye had the same involvement plus corneal haze and iritis.

At the end of one week the 1.0-mg. eye was

TABLE 4  
SUBCONJUNCTIVAL INJECTION 0.5 CC. TETRACYCLINE 10 MG./CC.  
(Concentrations in micrograms per cc.)

Time (hr.)	Intact Eye			Abraded Eye		
	Cornea	Aqueous	Vitreous	Cornea	Aqueous	Vitreous
1	19.0	6.0	3.0	88.0	37.0	5.0
2	23.0	2.0	0.0	83.0	12.0	0.0
4	2.0	1.0	0.0	13.0	0.7	0.0

TABLE 5  
CORNEAL BATH WITH TETRACYCLINE 25 MG./CC.  
(Concentrations in micrograms per cc.)

Time (hr.)	Intact Eye			Abraded Eye		
	Cornea	Aqueous	Vitreous	Cornea	Aqueous	Vitreous
1	54.0	2.0	0	41.0	14.0	0
2	38.0	2.0	0	34.0	3.0	0
4	1.0	0.0	0	3.0	1.0	0

clear, the 5.0- and 10-mg. eyes showed only slight congestion, and the 25-mg. eye was red, congested with a hazy cornea and iritis.

At the end of 10 days all eyes were clear except the 25-mg. eye which showed a slight corneal haze. At the end of 15 days this eye, too, became clear.

It may be concluded that subconjunctival injections even up to 25 mg./cc. in 0.5 cc. volume produce no permanent ocular damage but the severity of local reactions in concentrations above 5.0 mg./cc. would indicate that that level is the maximal safe dose.

## 2. EYE DROPS

Three times daily for three days two drops of solution were instilled into four normal rabbit conjunctival sacs. At night an ointment containing 10 mg./gm. was instilled in the sacs. The first eye received a concentration of drops of 1.0 mg./cc., the second 5.0 mg./cc., the third 10 mg./cc., and the fourth 24 mg./cc.

All eyes remained clear when observed at the end of one, two, three, and seven days. Obviously eye drops in concentrations up to 25 mg./cc. are harmless.

## 3. CORNEAL BATH

Four normal rabbit eyes were bathed for five minutes twice daily for three days. The concentration applied to the first eye was 1.0 mg./cc., the second 5.0 mg./cc. the third 10 mg./cc. and the fourth eye 25 mg./cc.

At the end of 24 hours the 1.0-mg. eye was clear, the 5.0-mg. eye was slightly congested, the 10-mg. eye was more congested and presented some secretion, and the 25-mg. eye had red swollen lids, thick red conjunctiva, slight secretion, and corneal haze.

At the end of 48 hours and again at 72 hours the 1.0-mg. eye was clear, the 5.0- and 10-mg. eyes were slightly congested, and the 25-mg. eye had swollen lids, red conjunctiva, secretion, and a completely cloudy cornea.

At the end of one week all eyes were clear except for the 25-mg. eye which presented corneal opacification and slight conjunctival congestion. The same picture was present at the end of 10 days. At the end of 15 days the corneal opacity of the 25-mg. eye was still present. Observations were then terminated.

It may be assumed that corneal baths in concentrations up to 10-mg./cc. are safe. In

TABLE 6  
EYE DROPS OF TETRACYCLINE 25 MG./CC.  
(Concentrations in micrograms per cc.)

Time (hr.)	Intact Eye			Abraded Eye		
	Cornea	Aqueous	Vitreous	Cornea	Aqueous	Vitreous
1	10.0	0.5	0	32.0	8.0	0
2	10.0	2.0	0	35.0	14.0	0
4	5.0	0.0	0	10.0	1.0	0

higher concentrations corneal opacification may result.

#### 4. INTRACAMERAL INJECTION

Injections of 0.1 cc. were made once into each of four normal rabbit anterior chambers. The first eye received a concentration of 1.0 mg./cc., the second 5.0 mg./cc., the third 10 mg./cc., and the fourth 25 mg./cc.

Twenty-four hours later the 1.0-mg. eye showed a fine pupillary membrane. The 5.0-mg. eye had a hazy cornea. The 10-mg. eye presented ciliary congestion and dense corneal opacity. The 25-mg. eye was severely congested with complete opacification of the cornea.

At the end of 48 hours the 1.0-mg. eye showed a fine membrane on the iris and the 5.0-mg. eye only slight infiltration of the cornea. The 10-mg. eye still had a ciliary flush and opaque cornea. The 25-mg. eye remained severely congested with an opaque cornea.

At the end of six days, the 1.0- and 5.0-mg. eyes were clear. The 10-mg. eye showed fine corneal opacities and posterior synechias. The 25-mg. eye remained congested with dense deep opacification of the cornea.

At the end of nine days all eyes were clear except for the 25-mg. eye which still showed corneal opacification plus cataract formation. The appearance of the latter eye remained unchanged up till observations were terminated at the end of 24 days.

Apparently intracameral injections of 0.1 cc. of 1.0 mg./cc. concentration are safe;

higher concentrations may produce temporary or permanent corneal opacities and even cataracts.

#### SUMMARY

1. Tetracycline is an effective antibiotic agent in vitro for the gram-positive bacteria but cross resistance with chlortetracycline and oxytetracycline is to be expected.

2. Aqueous levels theoretically effective against gram-positive organisms appear up to two hours after intravenous injections of 100 or 150 mg. in rabbits. Small corneal and smaller vitreous levels are found one hour after intravenous injection of 150 mg. The latter dose may, however, be near lethal.

3. Subconjunctival injections of 10 mg./cc. produce very adequate corneal and aqueous levels up to four hours and vitreous levels up to one hour. The inflamed eye accepts the antibiotic more generously than the normal eye.

4. Corneal bath or eye drops in concentrations of 25 mg./cc. produce very effective corneal levels for four hours. Aqueous levels are adequate up to two hours in the intact and up to four hours in the inflamed eye.

5. Subconjunctival injections in concentrations up to 5.0 mg./cc. are safe, eye drops in concentrations up to 25 mg./cc. are harmless, corneal baths in concentrations up to 10 mg./cc. are innocuous, and intracameral injections in concentrations greater than 1.0 mg./cc. are dangerous.

1601 Spring Garden Street (30).

#### REFERENCES

1. Booth, J. H., et al.: Tetracycline. *J. Am. Chem. Soc.*, **75**:5621 (Sept.) 1953.
2. Conover, L. H., et al.: Terramycin: XI. Tetracycline. *J. Am. Chem. Soc.*, **75**:4622 (Sept.) 1953.
3. Flippin, H. F.: The tetracyclines. *Philadelphia Med.*, **49**:733 (Jan.) 1954.
4. Finland, M., et al.: Clinical and laboratory observations of a new antibiotic, tetracycline. *J.A.M.A.*, **154**:561 (Feb.) 1954.
5. Brochure on Achromycin (tetracycline). Lederle Laboratories Division, American Cyanamid Company.
6. Brochure on Tetracyn (tetracycline). J. B. Roerig and Company.

## SIMPLIFIED METHOD OF CURARE ADMINISTRATION IN CATARACT SURGERY\*

OSCAR DAHLENE, M.D.

*Hattiesburg, Mississippi*

AND

J. WESLEY MCKINNEY, M.D.

*Memphis, Tennessee*

The use of curare in cataract surgery has not been universally accepted, possibly because of the fear of complications or the necessity for the assistance of an anesthetist for its administration. It is the purpose of this communication to present a simplified technique of curare administration which has eliminated the need for an anesthetist and has been without the slightest untoward reaction in 150 cases of cataract extraction.

The advantage of a quiet eye in a relaxed patient during cataract surgery needs no exposition. Curare is a valuable aid in securing this. The drug has for the ophthalmologist the happy property of paralyzing the muscles about the eye in lower dosages than are required for paralysis of the other skeletal muscles.

It has been found that increasing doses injected intravenously produce first paralysis of the eye and facial muscles and then in order, those of the pharynx, larynx, and extremities. As the dose is increased, the intercostal muscles and lastly the diaphragm are paralyzed. The paralysis of the ocular muscles occurs not only at a lower dosage but last longer than the paralysis of the other skeletal muscles. The effect on the ocular muscles of a single intravenous injection of curare reaches its maximum in about four minutes, continues for 20 to 25 minutes, and then falls off rapidly.

Kirby<sup>1</sup> and Clark<sup>2</sup> were the first to make use of this selective effect in ophthalmic surgery. Others have confirmed their ob-

servations. Cordes and Mullen<sup>3</sup> and Henderson<sup>4</sup> have reviewed the literature, giving a thorough coverage of the history of the discovery of curare and its evolution from a medical curiosity to a useful aid to ocular akinesia.

### MODE OF ACTION OF CURARE

The pharmacodynamics of curare have been extensively treated in previous publications.<sup>1, 3, 5</sup> We may summarize by noting that curare acts by way of the blood stream to eliminate the response of individual striated muscle fibers to the acetylcholine liberated at the myoneural junction. Very large doses block the response of smooth muscle fibers also.

It is interesting to compare this action with that of procaine. The latter has the property of blocking the production of acetylcholine at the myoneural junction. The paralysis produced by procaine may not be complete because of insufficient saturation of the nerve or because excessive nerve impulses from above may get through to the myoneural junction in the very apprehensive patient.

That the production of acetylcholine is not always completely suppressed by procaine injections is often observed clinically. Apparently effective O'Brien or Van Lint akinesia may not prevent squeezing of the lids from fright or painful stimulus. Retrobulbar injections of procaine regularly do not produce complete paralysis of the extraocular muscles even when reinforced by epinephrine and hyaluronidase.

The paralysis produced by curare is not affected by the greater production of acetylcholine from efferent motor impulses be-

\* From the Department of Ophthalmology, University of Tennessee College of Medicine, John Gaston Hospital, and Memphis Eye, Ear, Nose, and Throat Hospital, Memphis, Tennessee.

cause the muscle fibers are rendered incapable of contracting; however, much acetylcholine is produced at the myoneural junction. Thus, there is greater security in the paralysis produced by curare than in that produced by procaine.

Kirby,<sup>6</sup> Barraquer,<sup>7</sup> Henderson,<sup>4</sup> and others have depended entirely on curare for securing paralysis of the extraocular muscles. On the other hand, Cordes and Mullen<sup>8</sup> have merely added curare to their routine Van Lint akinesia and retrobulbar procaine injection.

To combine the action of curare and procaine seems logical, if, in fact, the two drugs act synergistically. No experimental evidence for this synergism could be found, but clinically it is readily demonstrable.

#### CLINICAL OBSERVATIONS

We were led to undertake the use of curare in cataract surgery by the evident advantages of its use as set forth by Kirby.<sup>6</sup> Initially no retrobulbar injection was used. Curare was injected by intravenous drip under the control of an anesthetist. One cc. was injected at a time at four-minute intervals until the desired effect was obtained. It was found that the average dose of curare necessary for the effective paralysis of the extraocular muscles ranged between three to four cc. of d-tubocurarine (3.0 mg. per cc. or 20 units per cc.) Occasionally five cc. and rarely even more than five cc. were required.

Preoperative medication consisted of 75 mg. of Demerol and 1/150 gr. of atropine given subcutaneously.

From time to time during the curarization and before the beginning of the operation, the patient was asked to look upward, downward, and horizontally. Upward movements were first abolished, then downward, and finally horizontal rotations. It was not considered necessary to abolish completely all horizontal rotation or the slight rotatory movement which usually remained.

No serious complication was encountered using this technique. It was noted,

however, that, on occasion, patients in whom four cc. or more were required complained of a mild sense of suffocation, which caused a little apprehension on the part of the patient and surgeon. The symptom always passed off quickly, however, and the patient was easily relieved by oxygen blown over the mouth under the drapes.

This inconvenience led us to resume the use of the retrobulbar injection of procaine epinephrine and hyaluronidase followed by injection of curare, one cc. at a time until the desired effect was obtained. It was soon apparent that only two to three cc. of curare were required rather than the usual three to four cc. when curare was depended upon alone.

Before beginning the injections of curare, the effect of the retrobulbar procaine was assessed. The patient's ability to rotate the eye on command was extremely variable. Individual responses varied from almost complete inability to rotate the eye in some cases to a response with wide excursions of the eye in others. Curare was then given, one cc. at a time. Although the dosage required was less, paralysis was the same as with curare alone.

In making our observations we soon ignored the orbicularis muscle, in view of the fact that the effect of curare on this muscle closely parallels its effect on the extraocular muscles. It is also more convenient to have the speculum in place while observing the ocular rotations. Furthermore, the tonus of the extraocular muscles is a much more important factor than contraction of the orbicularis in producing the expulsive force responsible for complications during the time that the eye is opened.

Since the reduced dosage of curare (two to three cc.), given one cc. at a time after procaine injections, had proved effective it was decided to try two cc., given at a single injection. This dose is one-half that which had been noted to cause a sense of suffocation in certain of those cases wherein curare was used without retrobulbar procaine. The



extraocular muscle paralysis produced by this rapid injection of low dosage proved to be equal to that produced by curare alone or retrobulbar procaine and curare administered more slowly.

Two parallel series of cases were then set up. In each series, two cc. of curare were injected at one time and no more. A total of 82 cataract extractions were performed using a rapid intravenous drip of curare in five-percent glucose solution. After all the curare had entered the vein, the drip was continued at a reduced rate throughout the operation, while the anesthetist sat by the patient. In the other series, 68 cataract extractions were performed wherein the curare was given as a single intravenous injection by the circulating nurse. Both methods were equally effective.

The antidote Tensilon (N-ethyl-M-hydroxyphenyl-N, N diethylammonium bromide) and oxygen were kept in readiness but never used. No untoward symptoms were noted in the 150 cases observed.

#### PRESENT TECHNIQUE

Curare has been considered by us to be merely an addition to the medications used for control of the eye and the patient to be operated upon. Premedication consists of three gr. of sodium amytal, 50 to 100 mg. of Demerol, and 1/150 gr. of atropine. Occasionally, in the case of a large, tense patient, an additional 50 mg. of Demerol is given intravenously along with the curare. The installation of cocaine (four percent) is begun in the patient's room and continued in the operating room. Routine O'Brien akinesia and retrobulbar injection of procaine, epinephrine, and hyaluronidase are performed.

The operation is begun immediately upon the completion of the retrobulbar injection. The conjunctival flap is dissected, and troublesome bleeding points cauterized. The superior rectus bridal suture is inserted and secured so as to rotate the eye to the position desired. When everything is ready for the

incision into the anterior chamber, two cc. of curare are injected rapidly into the vein of the arm.

Observations of the ocular rotations are no longer made. Since the effect of curare reaches its maximum within four minutes and lasts 20 to 25 minutes, the eye and the patient arrive at the maximum relaxation at about the time the sutures have been placed and the iridotomy completed. The surgeon, therefore, need not hurry because he can be sure of adequate time even if complications should arise.

#### COMMENTS

The outstanding advantages of curare administration are the immobility of the eye and the absence of expulsive force which it assures. It is entirely feasible, after the lens has been removed, to lift up the corneal flap and inspect the vitreous directly. The vitreous face may be found to be only slightly convex or even concave, indicating the absence of vitreous pressure. In no case have we seen vitreous well up and burst after the lens is removed, even in the very bad actors on our charity service. Remnants of a torn capsule may be grasped and removed under direct vision.

Collateral benefits of curare are a relaxed surgeon and an almost unconcerned patient. The intelligent patient who comes to the operating room awake despite the premedication and afraid that he might make a move during a crucial stage of the operation, loses his apprehension, relaxes, and may even go to sleep after the curare is injected.

The complete absence of untoward side reactions to the injection of two cc. of curare was gratifying. Patients operated upon ranged in age from 31 to 86 years. The usual degenerative conditions of the elderly were encountered. Two moderately severe asthmatics had no difficulty. Preoperative medication with 1/150 gr. of atropine prevented bronchospasm and excessive secretions. No cases of myasthenia gravis were seen.

Vitreous was lost in seven cases (4.7 per cent) of 150 cases operated upon. In none of these was forward movement of the vitreous body accountable for the loss. Rather, the loss was attributable to factors such as undue adhesion of vitreous face to lens (both eyes of same patient), surgical accidents, or temporary ineptitude of the surgeon.

#### CONCLUSIONS

Our observations on the use of curare in 150 cataract extractions confirm the opinion of others that it is a valuable adjunct for the better control of the patient who is to undergo cataract surgery.

A reduced dosage of curare (two cc.) acting synergistically with the procaine of the retrobulbar injection and O'Brien akinesia yielded effective relaxation of the extraocular muscles and eyelids. Preoperative sedatives plus curare yielded a completely relaxed patient. No untoward symptom was noted with the small dosage used (one-half the dose previously noted to cause a complaint of mild suffocation).

The services of an anesthetist are no longer considered necessary.

Hall Street.  
921 Exchange Building (3).

#### REFERENCES

1. Kirby, D. B.: Use of curare in cataract surgery. *Tr. Sect. Ophth. A.M.A.*, 1949, pp. 279-293.
2. Clark, W. B.: Use of curare as an adjuvant in cataract surgery. *Watson Gaily Eye Foundation Quart.*, 1:34, 1949.
3. Cordes, F. C., and Mullen, R. S.: The use of curare in cataract surgery. *Am. J. Ophth.*, 34:557-564 (Apr.) 1951.
4. Henderson, J. W.: Curare akinesia in cataract operations. *Am. J. Ophth.*, 36:781-788 (June) 1953.
5. Drucker, A. P., Sadove, M. S., and Unna, K. R.: Ophthalmic studies of curare and curarelike drugs in man. *Am. J. Ophth.*, 34:543-553 (Apr.) 1951.
6. Kirby, D. B.: Curare in cataract surgery: Five years' experience. *Tr. Sect. Ophth. A.M.A.*, 1952.
7. Barraquer Moner, J. I.: The present technic and results of the use of curare in ocular surgery. *Am. J. Ophth.*, 36:789-794 (June) 1953.

### INFLUENCE OF COFFEE UPON OCULAR TENSION\*

#### IN NORMAL AND IN GLAUCOMATOUS EYES

W. LEYDHECKER, M.D.

Bonn, Germany

We have been taught that glaucoma patients should not drink coffee because this would increase the ocular tension. In coffee drinking two factors could influence the tension, caffeine and water. The effect of water drinking upon the ocular tension has been the subject of many publications<sup>1-21</sup> and was studied in detail in my own communications.<sup>22-27</sup> Caffeine has been applied as a provocative test,<sup>28-30</sup> but the limits between physiologic and pathologic reactions of the tension have not been clear so that

evaluation of the test was difficult.

I have applied both the caffeine and the water-drinking tests to a number of persons with normal and glaucomatous eyes in order to prove their reliability and to study the hygienics of glaucoma.

#### EFFECTS OF CAFFEINE ON NORMAL EYES

In 198 eyes of 109 healthy subjects a provocative test with caffeine was performed. Five tests were done with 45 gm. of coffee in 150 cc. water, 11 tests with 0.5 gm. caffeine sodiobenzoate intravenously, and 182 tests with 0.4 gm. pure caffeine plus 150 cc. water.

\* From the University Eye Clinic, Director: Prof. H. K. Müller.

Tonometry was performed by me with the Schiøtz instrument before the test and every 15 minutes after the intake of caffeine for a period of one hour. The initial tension was in all cases below 30 mm. Hg (Schiøtz). Differences of the initial tension did not influence the result of the test.

The greatest difference between the tension before and after the test was taken in each case as the resulting variation of the tension. Its mean value was  $-0.4$  mm. Hg and the standard deviation was  $\pm 2.7$  mm. Hg. Details of the statistical analysis are given in a separate paper.<sup>37</sup>

I found that rise of 6.0 mm. Hg (Schiøtz) can be called a "probable pathologic result" (statistical probability 97.73 percent), and that a rise of 9.0 mm. Hg (Schiøtz) or more can be called a "definite pathologic result" (statistical probability 99.86 percent).

#### EFFECT OF WATER DRINKING ON NORMAL EYES

In 323 normal eyes of 171 healthy subjects the effect of drinking 1,000 cc. water in a state of fasting was studied. Tension was taken by me before the test and at 15-minute intervals after drinking. The time of observation was one hour and the drinking was done within five minutes. Differences of the initial tension, which was below 30 mm. Hg in all cases, did not affect the results. Details of the statistical analysis are contained in a separate paper.<sup>37</sup>

The mean variation of tension after the

test was  $+1.2$  mm. Hg and the standard deviation  $\pm 2.7$  mm. Hg. I can, therefore, call a rise of tension of 8.0 or 9.0 mm. Hg (Schiøtz) a "probable pathologic result" and a rise of 10 mm. Hg or more a "definite pathologic result."

#### EFFECT OF CAFFEINE ON GLAUCOMATOUS EYES

##### A. INITIAL TENSION 30 MM. Hg (SCHIØTZ) OR BELOW

A total of 226 tests with caffeine were carried out on 172 eyes with primary glaucoma (initial tension of 30 mm. Hg or below) which had not been operated upon. The technique was the same as that used in normal eyes. In order to avoid starting the test during a spontaneous rising or falling phase of tension, the tension was taken 30 minutes before and immediately before the test, which was started only if both readings did not differ more than 3.0 mm. Hg. This precaution was also taken in the other tests to be outlined later.

In 40 tests 45 gm. coffee in 150 cc. water were given; in 24 tests 0.5 gm. caffeine sodiobenzoate were injected into the cubital vein; and 162 tests were performed with 0.4 gm. pure caffeine with 150 cc. water by mouth.

The results are summarized in Table 1, in which the 226 tests are arranged according to the clinical form of glaucoma and also according to the width of the chamber angle.

TABLE 1  
RESULTS OF CAFFEINE TEST IN NONOPERATED GLAUCOMATOUS EYES  
(Initial tension 30 mm. Hg Schiøtz or below)

Form of Glaucoma	No. of		% Pathologic Tests		% Eyes with Pathologic Reactions	
	Tests	Eyes	Probable	Definite	Probable	Definite
Simple	137	106	8.7	2.2	9.4	2.8
Chronic congest.	77	57	6.5	11.7	7.0	15.8
Acute (interval)	12	9	0	0	0	0
Wide-angle	141	101	5.7	5.7	4.0	7.9
Narrow-angle	79	67	11.4	5.1	14.9	6.0
Width of angle not noted	6	4	0	0	0	0
Together	226	172	7.5	5.3	8.1	7.0

TABLE 2  
RESULTS OF CAFFEINE TEST IN NONOPERATED GLAUCOMATOUS EYES  
(Initial tension above 30 mm. Hg Schiøtz)

Form of Glaucoma	No. of		* Pathologic Tests		* Eyes with Pathologic Reactions	
	Tests	Eyes	Probable	Definite	Probable	Definite
Simple	29	22	0	3	0	4
Chronic congest.	21	17	4	2	3	1
Acute (interval)	1	1	1	0	1	0
Wide-angle	29	24	1	2	1	2
Narrow-angle	17	13	3	3	2	3
Width of angle not noted	5	3	1	0	1	0
Together	51	40	5	5	4	5

\* The number of eyes and tests is given in each group, since the total numbers are too small for calculation in percentages.

All cases in which there were no objective or subjective symptoms of congestion (headache, halos) have been classified as glaucoma simplex. The chamber angle was called "wide," if the ciliary-body band were visible in at least half of its circumference, and "narrow" if it were not visible. Only eyes with primary glaucoma are considered in this paper. Pathologic results were obtained in 15 percent of the eyes, and rises in tension of 9.0 mm. Hg or more occurred in only seven percent.

#### B. INITIAL TENSION ABOVE 30 MM. HG (SCHIØTZ)

A total of 51 tests were done on 40 eyes with primary glaucoma which had not been operated upon. The incidence of positive results was insignificantly greater than in

eyes with an initial tension below 30 mm. Hg (table 2). There were 11 tests with 45 gm. coffee in 150 cc. water; eight tests with caffeine sodiobenzoate (0.5 gm. intravenously); and 32 tests with pure caffeine (0.4 gm. by mouth).

#### EFFECT OF DRINKING WATER ON GLAUCOMATOUS EYES

There were 340 water-drinking tests carried out, with 1,000 cc., on 222 eyes with primary glaucoma which had not been operated upon. The mechanism and technique of this test have been described in previous reports<sup>22, 24, 27</sup> and most of the present material has been evaluated in a recent paper.<sup>27</sup>

It will be seen from Table 3 that this test gives a higher incidence of pathologic results as compared with the caffeine test. In eyes

TABLE 3  
RESULTS OF WATER-DRINKING TEST IN GLAUCOMATOUS EYES  
(Initial tension 30 mm. Hg Schiøtz or below)

Form of Glaucoma	No. of		% Pathologic Test		% Eyes with Pathologic Reaction	
	Tests	Eyes	Probable	Definite	Probable	Definite
Simple	213	139	4.2	18.8	4.3	24.4
Chronic congest.	105	72	10.5	16.2	13.9	25.0
Acute (interval)	22	11	4.5	22.7	0	45.5
Wide-angle	170	106	5.9	18.2	6.6	24.5
Narrow-angle	126	79	7.2	21.4	7.6	31.7
Width of angle not noted	44	37	4.5	9.1	8.1	16.2
Together	340	222	6.2	18.2	7.2	25.7

TABLE 4  
COMPARISON BETWEEN CAFFEINE TESTS AND WATER-DRINKING TEST IN 164\* EYES

Form of Glaucoma	Caffeine - Water -	Caffeine + Water +	Caffeine + Water -	Caffeine - Water +
Simple	66	3	9	25
Chronic congest.	28	7	6	11
Acute (interval)	7	0	0	2
Wide-angle	61	5	6	24
Narrow-angle	36	5	9	14
Width of angle not noted	4	0	0	0
Together	101	10	15	38

\* There are 164 glaucomatous eyes with an initial tension of 30 mm. Hg (Schiotz) or below, in which both tests have been done separately on a different day. The number of eyes is given in each group.

with an initial tension above 30 mm. Hg, the percentage of pathologic reactions is considerably greater, 77 percent.

#### DISCUSSION

The caffeine test is very unreliable as a provocative test in glaucoma. The percentage of eyes with initial tension of 30 mm. Hg or below which gave pathologic results after repeated provocation was as low as 15 percent. The water-drinking test is nearly twice as reliable and gives pathologic results in 33 percent glaucomatous eyes in the same tension group, if both probable and definite pathologic results are considered.

In 164 such eyes both tests were applied separately on different days (table 4). It was found that the water-drinking test was positive in 38 eyes in which the caffeine test had been negative, while the caffeine test was positive in only 15 eyes with a negative water-drinking test. It may therefore be concluded that the mechanism of both tests is different. This is further demonstrated by the fact that the caffeine test is only insignificantly more reliable in glaucomatous eyes with an initial tension above 30 mm. Hg than it is in those eyes with a lower tension; while, with the water-drinking test, the percentage of pathologic reactions increases with increasing initial tension.

For the hygienics of glaucoma, the total percentage of pathologic reactions is not so important as the percentage of abrupt rises in ocular tension, which I have termed

"definite pathologic reactions." These occurred with caffeine in seven percent and with water in 25.7 percent of the eyes with an initial tension of 30 mm. Hg or less. This difference shows clearly that caffeine is harmful in a small percentage of glaucoma patients only, while water definitely affects the tension of a quarter of these patients.

In a previous paper,<sup>22</sup> it was shown that with 500 cc. of water, the osmotic changes occurring in the blood are only slightly less than those observed after 1,000 cc. and that pathologic rises of the ocular tension frequently occur with this amount of water.

From these observations, it may be concluded that the ingestion of larger quantities of fluid is more dangerous for glaucoma patients than is caffeine. This view is in accordance with Kolb's findings.<sup>26</sup> We should therefore, first of all advise our patients to avoid larger quantities of fluid. This would probably apply to soup or alcoholic drinks just as well as to coffee. From this point of view, it would seem better to drink one cup of strong coffee (which contains less caffeine [0.1 gm.] than was used in my tests) than several cups of a weak brew, and better to drink more concentrated alcoholics than beer, for example, of which larger quantities are required to produce the same degree of psychologic stimulation.

Coffee should not necessarily be forbidden in all cases. If it is hard for a patient to give up coffee, I do two provocative tests with 0.4 gm. pure caffeine (which is approxi-



mately the amount of coffee contained in 45 gm. coffee) on different days. If there is no "definite pathologic rise" of tension during the test, the patient is allowed to have coffee but is advised to take only one cup at a time, which contains only 0.05 to 0.1 gm. caffeine, and which most probably will never be harmful.

#### SUMMARY

A large number of caffeine or water-drinking tests have been done in healthy and glaucomatous subjects. The caffeine test is less

reliable in glaucoma than the water-drinking test. In a series of 164 glaucomatous eyes with initial tensions below 30 mm. Hg, both tests were applied separately and on different days.

It is concluded from the results that patients suffering from glaucoma should be advised to avoid drinking large quantities of any fluid, although it does not appear necessary to forbid coffee in small quantities in all cases. It is best to advise each individual patient after doing the caffeine test.

*Wilhelmstrasse 31.*

#### REFERENCES

1. Schmidt, K.: Untersuchungen über Capillarendothelstörungen bei Glaucoma simplex. Arch. Augenh., **98**:569, 1928.
2. ———: Klinische und experimentelle Studien über lokale und allgemeine Gefäßstörungen beim Glaucoma simplex. Arch. Augenh., **100/101**:190, 1929.
3. ———: Trinkversuch und Glaukomproblem. Arch. Augenh., **104**:102, 1931.
4. ———: Die Belastung des Glaukomauges in Diagnose und Therapie. Klin. Monatsbl. f. Augenh., **116**:614, 1950.
5. de Decker, J. F.: Ueber den Einfluß der Plasmavermehrung auf den normalen Augendruck. Arch. Augenh., **100/101**:180, 1929.
6. Poos, F.: Klinische Untersuchungen über die Beziehungen zwischen Osmose, Blutdruck und Augendruck. Klin. Monatsbl. f. Augenh., **84**:340, 1930.
7. Wegner, W.: Untersuchungen über Zusammenhänge zwischen Wasserhaushalt und Glaukom. Ber. Deutsch. ophth. Ges. Heidelberg, **48**:127, 1930.
8. Gradle, H. S.: Concerning simple glaucoma, Amer. J. Ophth., **14**:936, 1931.
9. Heegard, S., and Larsen, V.: Einiges über den Wasserstoffwechsel bei Normalen und Glaukomkranken. Acta Ophth., **9**:302, 1931.
10. Spadavecchia, V.: Influenza della prova di carico idrico sulla pressione arteriosa generale e sul tono oculare. Ann. Ottal., **64**:611, 696, 1936, and **65**:194, 1937.
11. Ohm, G.: Glaukomproblem und Belastungsversuche. Das intermittierende Glaukom. Arch. f. Ophth., **135**:537, 1936.
12. Majorova, O. A., and Glinika, E. S.: Vest. Oftal., **15**:120, 1939. Abstracted in Zentralbl. f. Ophth., **45**:352, 1940.
13. Meves, H.: Das Verhalten des Augeninnendruckes nach Wasseranreicherung des Körpers durch Pituglandol. Arch. f. Ophth., **142**:41, 1941.
14. Tikhomirov, P. H.: Vest. Oftal., **16**:127, 1940. Abstracted in Zentralbl. f. Ophth., **46**:589, 1941.
15. Evans, J. N.: Diagnostic aids in the study of glaucoma. Arch. Ophth., **27**:1177, 1942.
16. Bloomfield, S., and Kellermann, L.: The relative value of several diagnostic tests for chronic simple glaucoma. Amer. J. Ophth., **30**:869, 1947.
17. Sugar, H. S.: The provocative tests in the diagnosis of the glaucomas. Amer. J. Ophth., **31**:1193, 1948.
18. Weinstein, P.: Evaluation of recent provocative tests for preglaucoma. Amer. J. Ophth., **33**:1442, 1950.
19. Honigsmund, R.: Ueber die klinische Bedeutung des Trinkversuches nach Marx unter besonderer Berücksichtigung der Frühdiagnose des grünen Stars. Thesis, Münster, 1951.
20. Rohrschneider, W.: Die Diagnose des beginnenden chronischen Glaukoms in der Sprechstunde. Bücherei des Augenarztes. Stuttgart, Enke, 1952, Heft 21, p. 53.
21. Argawal, L. P., and Sharma, C. K.: Two provocative tests for glaucoma. Brit. J. Ophth., **37**:330, 1953.
22. Leydhecker, W.: The water-drinking test. Brit. J. Ophth., **34**:457, 1950.
23. ———: The permeability of the blood-aqueous barrier to fluorescein during the water-drinking test in glaucomatous eyes. Brit. J. Ophth., **34**:480, 1950.
24. ———: Belastungsproben als Mittel zur Analyse der Funktionsstörungen beim primären Glaukom. Klin. Monatsbl. f. Augenh., **121**:174, 1952.

25. ———: Die Wassertrinkprobe bei Netzhautablösung. *Klin. Monatsbl. f. Augenh.*, **122**:272, 1953.
26. ———: Belastungsproben bei Glaukom. In Löhlein: *Zeitfragen der Augenheilkunde*. Leipzig, Thieme, 1954.
27. ———: Evaluation of the water-drinking test. *Brit. J. Ophth.*, **38**:290, 1954.
28. Löhlein, W.: Discussion. *Ber. Deutsch. Ophth. Ges. Heidelberg*, **38**:159, 1912.
29. Thiel, R.: Die physiologischen und experimentell erzeugten Schwankungen des intra-ocularen Druckes im gesunden und kranken Auge. *Arch. f. Augenh.*, **96**:331, 1925.
30. Wegner, W.: Massagewirkung und Stauungsversuche an gesunden und glaukomatösen Augen. *Zentralbl. f. Augenh.*, **55**:381, 1925.
31. von Sallmann, L., and Deutsch, A.: Die klinische Bedeutung der Tagesdruckkurve und der Belastungsproben bei Glaukom. *Arch. f. Ophth.*, **124**:624, 1930.
32. Federici, E.: Sul valore clinico della prova della caffeina per la diagnosi precoce del glaucoma cronico semplice. *Boll. ocul.*, **11**:752, 1932.
33. Stein, R.: Ueber den klinischen Wert der Belastungsproben für die Glaukomdiagnostik. *Med. Klin.*, **29**:1235, 1933.
34. Gilde, J.: Untersuchungen über die Wirkung des Pilocarpins, Homatropins und Kaffees auf den intraocularen Druck des normalen Auges als Grundlage für die Diagnostik des latenten Glaukoms. Thesis, Königsberg, 1937.
35. Brinke, G.: Untersuchungen über die Verwertbarkeit der Coffeinbelastung als Frühdiagnose des Glaukoms. Thesis, Münster, 1950.
36. Kolb, H.: Ueber die Wirkung von koffeinhaltigem, koffeinfreiem Kaffee und Wasser auf das glaukomkranke Auge. *Klin. Monatsbl. f. Augenh.*, **121**:524, 1952.
37. Leyhecker, W., and Niesel, P.: Statistische Berechnung der physiologischen Grenzwerte bei Glaukombelastungsproben. *Klin. Monatsbl. f. Augenh.*, **125**:458, 1954.

## FLICKER-FUSION FREQUENCY AND HYPERTENSION\*

JORDAN M. SCHER, M.D.

*Baltimore, Maryland*

AND

WILLARD H. SPANKUS, M.D.

*Houston, Texas*

The vigorous assault against hypertension in recent years has necessitated more discriminating techniques for its early recognition. Many methods have been proposed for discovering those whose altered vascular reactivity may indicate imminent hypertensive disease. Among these have been the cold-pressor test<sup>1</sup> and, more recently, the reaction to hypertensive agents.<sup>2</sup> The use of flicker fusion as an index of vascular tonus is based on reports of its variation in circulatory insufficiency,<sup>3</sup> central nervous-system fatigue,<sup>4</sup> and during drug administration.<sup>5,6</sup> Krasno and Ivy<sup>7</sup> have studied

flicker fusion frequency in coronary and hypertensive diseases.

Following publication of the article by Krasno and Ivy, it was hoped, in the light of their report, that the flicker-fusion technique might prove a method of anticipating acute cerebral vascular spasm. Thus treatment could be initiated before the process became clinically apparent. Since it soon developed that we were not able to reproduce their findings, an attempt to validate them or to determine the errors inherent in the method became the immediate concern of the investigation.

It is, therefore, the intention of this paper to present further data on the use of flicker fusion in discriminating between groups of hypertensive and normotensive individuals, and to examine several factors

\* From the Research Division of the Cleveland Clinic and the Frank E. Bunts Educational Institute, Cleveland, Ohio. Presented in part before a meeting of the Research Division of the Cleveland Clinic, September 16, 1950, in Cleveland, Ohio.

limiting its usefulness. Certain aspects of the physical and physiologic properties of the flicker phenomenon must be reviewed, since they affect the interpretation of this test, which, while simple enough in practice, is highly complex in principle.

#### LITERATURE REVIEW

If one increases the rate at which a light flickers, a critical threshold characteristic for each individual will be reached, beyond which the flicker appears to fuse and is registered in consciousness as continuous. Increasing the intensity of the light increases the number of flickers perceived before fusion occurs.<sup>8, 9</sup>

A larger target light source also raises the critical fusion value.<sup>10</sup> Decrease in pupil aperture decreases flicker fusion over short test periods.<sup>11</sup> The dark-adapted eye has a lower critical fusion frequency than one light-adapted.<sup>12</sup>

The threshold for fusion will fall if the field surrounding the target is much darker or brighter than the light source.<sup>12, 13</sup> Optimal discrimination of the point of fusion is achieved when the background has about the same intensity as the test light.<sup>14</sup> Sensitivity is greatest when the light phase is shorter than the dark in the flicker cycle.<sup>15</sup>

Recognition of a flickering light in consciousness depends on several known factors independent of its physical properties. According to Hecht,<sup>16</sup> the retinal receptors for flickering light stimuli are probably the cones. One evidence of this is that the color "orange" requires the briefest exposure for flicker identification by dark-adapted or light-adapted eyes.<sup>17</sup> Foveal fusion is less sensitive than that of the surrounding macula, but aberrations in acuity, refractive surfaces, and media do not seem to affect adversely flicker perception.<sup>18</sup>

Glaucoma and diabetic and arteriosclerotic retinopathy reduce the flicker-fusion threshold and the consistency of the test.<sup>19</sup> Chiasmal lesions alter flicker, as do lesions in the parietal lobe.<sup>20</sup> Ablation of the visual

cortex about the calcarine fissure does not seem to interfere with flicker transmission in monkeys<sup>21</sup> although it may reach a dead-end in awareness. Precise cerebral localization for flicker discrimination has not been achieved.<sup>10</sup>

In a very large series of subjects, flicker fusion was not apparently influenced by wakefulness as long as 112 hours<sup>22</sup> and, in a much shorter series,<sup>23</sup> it was not influenced by hard work over a one-hour period. Old age does not necessarily reduce it,<sup>11</sup> but hypothyroidism,<sup>24</sup> circulatory insufficiency,<sup>25</sup> and tobacco are said to reduce the critical fusion value.<sup>26</sup> A positive correlation with intelligence has been tentatively reported.<sup>26</sup>

Hypoxia at arterial saturations of 70 and 80 percent have been said to produce no striking change,<sup>27</sup> although re-breathing into a bag reduced fusion threshold after two minutes in several patients tested by us. Flicker fusion has been found to vary 0.6 percent in the most consistent and 2.0 percent in the least steadily responsive subjects from day to day.<sup>23, 28</sup>

Variations<sup>18</sup> of two to three flashes per second are generally not considered significant in the macular area of each eye, and there may be differences of as many as five flashes per second between the two eyes. Peripheral field critical fusion value, however, should be almost identically reproducible bilaterally. The perifoveal area to the 20-degree tangent is some five flashes higher than the foveal beyond which peripheral retinal critical fusion value declines from the 30- to 100-degree tangent.

#### METHODS

This study may be conveniently divided into two parts. Part I provides an experimental evaluation of the Krasno-Ivy nitroglycerin flicker method. Part II is an experimental attempt to study the roles of retinal vasculature and pupil aperture in the interpretation of changes in critical fusion value.

The patients, on whom statistical studies

were made, include 46 with hypertension of varying severity and 51 normal control subjects. The controls were chosen because of their freedom from peripheral vascular disease; blood pressures below 140 mm. Hg, systolic, and 90 mm. Hg, diastolic; and normal eyegrounds, cardiac status, and renal function.

The hypertensive patients included seven with grade IV eyeground changes, nine with Grade III, nine with Grade II, and 17 with Grade I, and four with no change. One patient with Grade III eyegrounds had lupus erythematosus.

The method was that of Krasno and Ivy,<sup>7</sup> modified in detail. In order to achieve better control values, more determinations were taken; initially, one per minute for a control series of six minutes and a similar number following administration of fresh nitroglycerin sublingually in doses of 1/100 gr. Since the flicker-fusion rate has been reported to be unmodified by learning, or training,<sup>18</sup> a rundown of the frequency scale was performed for each patient to acquaint him with what was expected. This, plus a few words, made training almost immediate. The patient was instructed to say "flick" when he just received the transition from a continuous light to a flickering one.

The criteria for a positive test were those stipulated by Krasno and Ivy,<sup>7</sup> except that the results were translated into flashes per second in accordance with standard usage, rather than flashes per minute as preferred by them.

Tobacco was withheld for at least one hour before the test, although the elevation in flicker-fusion frequency following smoking has been reported to return almost to the base line 15 to 20 minutes afterward.<sup>25</sup> A rest of one-half to one hour preceded each run. The tests were conducted in an air-conditioned and sound-proofed room, since noise is said to affect flicker fusion rate.<sup>20</sup>

That the systemic effects of nitroglycerin might be evaluated, blood-pressure by the cuff method and pulse readings were made

concurrently with flicker exposures, and were used as criteria of the efficacy of the drug. An attempt to correlate blood pressure, pulse rate, and flicker fusion was made in this series.

In 28 subjects, ophthalmoscopy was employed without success to observe the arteriolar changes said to follow nitroglycerin, and was discontinued for this purpose. It was continued in the hypertensives for purposes of classification.<sup>31</sup>

Retinal photography in all patients was utilized to provide objective evidence of the proposed variations in arteriolar or venular caliber over a six-minute period following nitroglycerin (fig. 1).

Because of the previously known effect of pupil size<sup>8, 9, 11</sup> on flicker fusion and apparent changes observed by us, pupillary photography, under the lighting conditions stipulated in the Krasno-Ivy nitroglycerin flicker-fusion test, was employed to record objectively the presence of these changes. The test, as already stated, was also conducted on several patients with stellate-ganglion block alone, and others in whom homatropine mydriasis was superimposed upon the block.

## RESULTS

### PART I

The clear-cut results reported by Krasno and Ivy were not substantiated by this study (table 1). In 21 normals (41 percent) and 28 hypertensives (61 percent), no change was perceived following nitroglycerin. Twenty-five normals (49 percent) and 12 hypertensives (26 percent) reacted with a flash increase in rate before fusion. Five (10 percent) normals and six (13 percent) hypertensives reacted with a flash decrease before fusion occurred. Those hypertensives with Grade III and Grade IV eyeground changes had slightly lower initial critical fusion value than the hypertensives with Grades I and II or no apparent fundus changes, and tended to reduce the group average critical fusion value. The entire group of hypertensive pa-

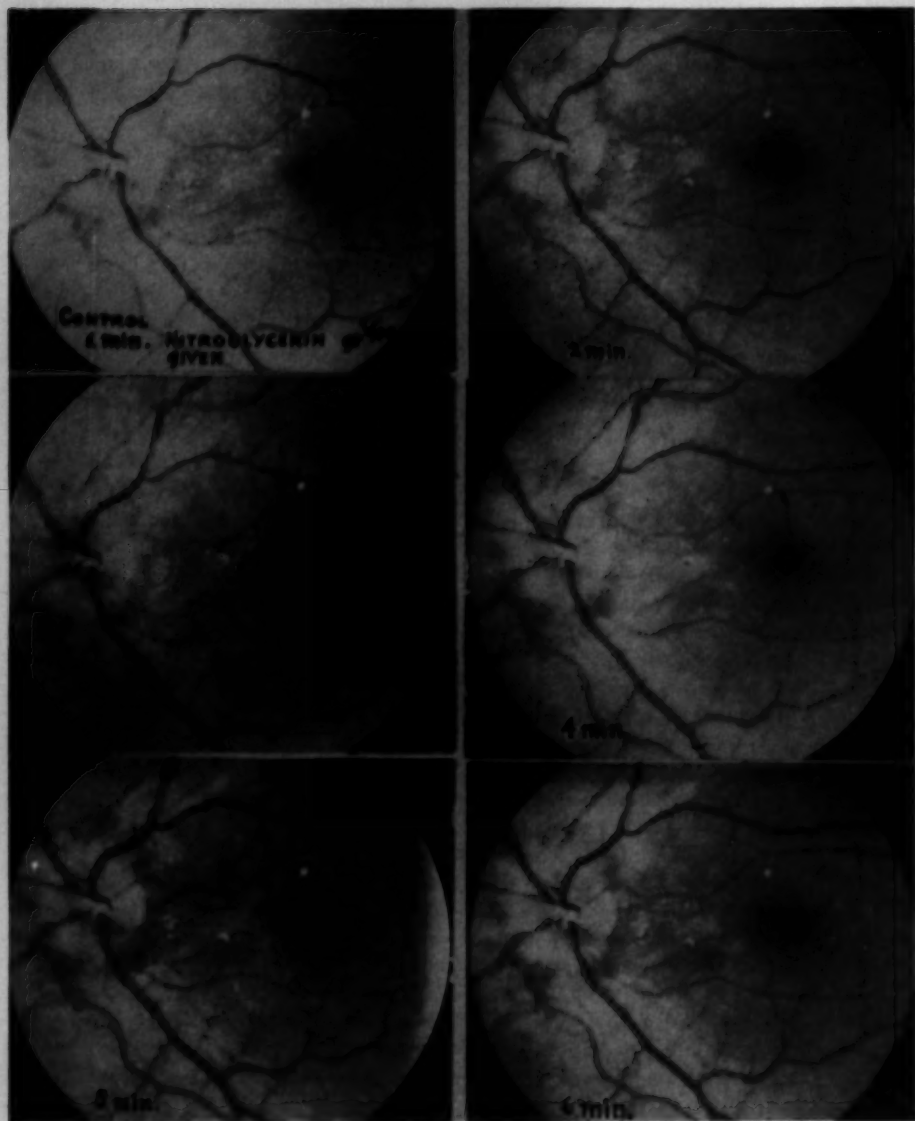


Fig. 1 (Scher and Spankus). Retinography before and after nitroglycerin in a hypertensive patient whose flicker-fusion threshold improved one flash per second following administration of the drug. No measurable vascular changes are evident.

tients, including the more severe, showed no other characteristic or directional critical fusion value change following nitroglycerin, except as noted.

Statistical analysis of these data failed to show any significance in discriminating between the pre- and postnitroglycerin critical fusion value for each group, and for the



TABLE 1

SIMULTANEOUS AVERAGE NITROGLYCERIN FLICKER-FUSION TEST, BLOOD-PRESSURE AND PULSE CHANGES

Normal Subjects 51 (100%)			
NG/FFT*	Increase	Decrease	No Change
	25 (49%)	5 (10%)	21 (41%)
Blood Pressure (average change)			
Systolic	-14.9	+ .4	+ 9.6
Diastolic	- 2.0	- 5.4	- 1.4
Pulse (average change)	+ 3.6	+10.5	+13.9
Hypertensive Subjects 46 (100%)			
NG/FFT	Increase	Decrease	No Change
	12 (26%)	6 (13%)	28 (61%)
Blood Pressure (average change)			
Systolic	-26.7	-27.1	-19.5
Diastolic	- 1.4	- 7.1	- .31
Pulse (average change)	+16.9	+15.3	+15.07

\* NG/FFT indicates critical fusion value change (increase, decrease, no change) following nitroglycerin administration. Corresponding simultaneous average blood pressure and pulse changes, with the direction of change for each group, is compared. The + or - sign indicates the direction of change. Critical fusion value change accepted as one flash per second, as stipulated by Krasno and Ivy.

combined groups, since the difference between the means is less than twice the standard error of the difference between the means. It further indicated the better-than-chance possibility that the results were well within the range of normal variation (table 2).

The same patterns of response followed subsequent testing of other subjects not included in the analysis. In all subjects who, on one dose of nitroglycerin, failed to yield flicker changes despite evident systemic variations, a second dose was given, but only rarely succeeded in effecting a response. It is interesting that the flicker trends are more or less parallel for both groups.

Following nitroglycerin administration, blood-pressure decreases to 20 to 25 mm. Hg systolic were noted in almost all of the hypertensives; to a lesser degree, this occurred in the normotensive patients.<sup>22, 23</sup> Several of the normotensives, particularly those with pressures below the average for their age group, had elevations in pressure as high as 5.0 to 15 mm. Hg, systolic, and 5.0 to 10 mm. Hg, diastolic, two minutes after nitroglycerin, which subsequently declined to lower systemic values in accordance with the normal pattern.

Pulse rates rose five to 20 beats per minute, two minutes after nitroglycerin, returning to normal usually within the period of the test. The average pulse rates increased more in the hypertensives than in the normotensives. A characteristic reaction to nitroglycerine was observed to a greater or lesser extent in both groups. Flushing was noted in the malar areas and forehead. Respiratory rate was increased, with deeper breathing. Most of the patients complained

TABLE 2  
STATISTICAL EVALUATION OF NITROGLYCERIN FLICKER-FUSION TEST

		Before Nitroglycerin Flashes/Sec.	After Nitroglycerin Flashes/Sec.	Difference Means	S.E. Difference Means	Coefficient (%) ± Variation	Significance
Normal	Mean	37.58	37.98	0.40	1.31	3.48	0.57
	Number	46	46				
Hypertensive	Mean	40.43	40.97	0.54	1.51	3.85	0.55
	Number	51	51				
Combined	Mean	39.07	39.55	0.48	0.701		
	σ Number	3.95 97	4.28 97				

after about two minutes of slight "giddiness," "light-headedness," "pounding of the temples," "full feeling" in the chest, or a heaviness or numbness of the arms, less often the legs. A general feeling of warmth was occasionally mentioned. No gastric or neuropsychiatric symptoms appeared.

#### COMPLICATIONS

Seven patients collapsed following nitroglycerin administration: Three normotensives and four hypertensives. One of the hypertensive patients was on nitroprusside therapy, another had lupus erythematosus. Each reaction was marked by a fall in the diastolic pressure of 0 to 30 mm. Hg, and the systolic of 60 to 90 mm. Hg, depending on the initial blood pressure. Recovery occurred rapidly after several minutes in the supine position in each case.

In one normotensive, clonic twitching of the hands occurred, which may have represented a latent convulsive tendency facilitated by nitroglycerin;<sup>34</sup> it was followed by syncope and urinary incontinence. The lupus patient also demonstrated clonic hand movements. A 51-year-old essential hypertensive Negro on veriloid therapy, who was rendered unconscious by a second dose of nitroglycerin, complained of recurrent "weak spells" for two days thereafter, but blood pressure and pulse did not vary from usual during that period. No other morbidity occurred.

#### PART II

It was not possible to demonstrate vascular changes in the human retina following nitroglycerin administration by ophthalmoscopic examination and the serious effort to do so was discontinued after 28 patients had been carefully observed in a dark room following 10 to 20 minutes of adaptation. This was further documented by retinal photography in 11 patients. Nitroglycerin, 1/100 gr., was administered sublingually following a control picture and failed to produce objectively measurable vascular

changes in the visible retinal vessels over a six-minute period of observation (fig. 2).

Pupil photography was conducted upon 12 hypertensive subjects and eight normal individuals with and without the administration of nitroglycerin. A uniform response to fixed convergence at a distance corresponding to the test, or about six feet, resulted in progressive contraction in 14 of these subjects of 0.5 to 1.0 mm. in transverse pupillary diameter in the absence of nitroglycerin over a period corresponding to that of the test (fig. 2).

Six failed to show miosis. Three of those demonstrating miosis over the six-minute period, presented as much as 0.5-mm. dilatation over the control value on the two-minute picture. Several individuals tested showed a remarkably rapid and strong contraction.

It was apparent in two hypertensive and three normal subjects previously given the nitroglycerin flicker-fusion test that, when flicker fusion tests were run following homatropine dilatation, an increased threshold occurred which could be explained on the basis of pupil size. Subsequent administration of nitroglycerin was without further effect on the fusion rate.

Conversely, stellate-ganglion block, productive of miotic pupils, gave lower flicker thresholds than control values in these patients, and again the results could be explained on pupil size alone. The administration of nitroglycerin following block did not apparently induce an independent effect.

When the mydriatic was superimposed upon the stellate block, similar results to those following the mydriatic alone were encountered and giving nitroglycerin did not add separately to the results. Criteria for the assimilation of nitroglycerin remained the same in the course of these tests.

Efforts to fatigue the flicker phenomenon by rundowns on the Krasno-Ivy flicker-fusion photometer repeated as often as two to four times a minute for six to 10 minutes were not successful. Comments made by

**Case I****Case II****Case III**

Fig. 2 (Scher and Spankus). Pupil photographs taken under conditions of the Krasno-Ivy critical fusion value change following nitroglycerin administration at two-minute intervals, omitting the administration of nitroglycerin. Note the progressive miosis, which alone is capable of altering the flicker-fusion threshold by reducing light intensity.

patients during these tests indicated that the initial perception of flicker occurred at a corner or along a side of the target before appearing over the entire screen. This may

well have indicated that immediate centri-foveal fixation was not being achieved and that the more sensitive perifovea was receiving the earliest flashes.

## DISCUSSION

Before flicker fusion can be used clinically in hypertension or other medical conditions, there must be a much clearer understanding of the phenomenon itself. Many physical variables upon which it is dependent have already been noted, but the primary receptors, pathways, and critical limitations are still uncertain.

Undoubtedly blood supply, in a general way, is important here as elsewhere, but retinal vascular alterations have not been demonstrated to alter flicker fusion specifically either in the literature or in our observations. Localized vascular spasm is further not necessarily an indication of generalized disease.<sup>38</sup> According to Ragnar Granit, the limiting factor in flicker-fusion frequency is probably neuronal transmission, rather than blood supply.<sup>39</sup>

Pupil size must be emphasized in interpreting flicker fusion since this controls light intensity which is directly related to the fusion threshold. Under the conditions of this test, the subject may voluntarily increase the tension of accommodation inducing a constriction of the pupil without change in convergence in order to fix an object better<sup>37, 38</sup> by stare or attention, as we have also indicated.

Pupillary dilatation may be provoked by anemia, hypoxemia, and asphyxiation,<sup>39</sup> or cortical stimulation of area 8 in monkeys.<sup>40</sup> Pupil size also varies with the angle at which light strikes the retina.<sup>41</sup>

Amyl nitrite has been reported to induce pupillary dilatation,<sup>42</sup> which Gellhorn felt was secondary to its reduction of the blood pressure. This may have accounted for the transient dilatation in several patients on pupil photography, corresponding generally to the point of maximum activity of the nitroglycerin systemically.

Weekers, according to Miles,<sup>11</sup> reported that where decreased flicker fusion occurred with age, it was probably due to decreased pupil size. Since there seems to be a miosis

of the pupil with increased attention and reported dilatation following nitrite administration, flicker changes during the course of the test are quite possibly unreliable in view of mechanisms which appear to offset or compensate for one another.

The precise physiologic activity of the nitrites on various types and sizes of blood vessels is still uncertain. In 1914, Hirschfelder,<sup>43</sup> reported dilatation of "vessels" in the cat's retina and meninges following amyl nitrite by direct observation, and Wilkins<sup>44</sup> demonstrated that the nitrites dilated the venules of the skin without dilating its arterioles.

In view of the apparent effect of the nitrites on pupil size already noted,<sup>42</sup> and possibly its action on other as yet unrecognized elements of the visual mechanism, no single site of action may be said to be critical at the present time. Again the vagaries of mucosal absorption make standardization of dose and effect difficult. Individual sensitivity also may reduce the value of the test.

The present test specifically neglects contrast background which is felt to be important by Hylkema.<sup>44</sup> It does not fully fill the stipulations noted by Miles<sup>10</sup> for targets smaller than 1.5 cm. which necessitate perfect central fixation, intense light, and no ametropia for accurate flicker-fusion determinations.

It was interesting to note that in the fatigue runs, and those at one-minute intervals, adjacent readings occasionally differed by one flash or more per second without any drug. Thus the single-flash change established as critical by Krasno and Ivy seems to be within the normal range of variation.

In order to achieve reliably reproducible results from laboratory to laboratory, it would be desirable that instrumentation incorporating the following features be standard. Provision should be made for:

1. Calibration at and about 40 cycles per second of the flicker-rate generator before



a series of runs and as often as required thereafter to ascertain the constancy of frequency calibration.

2. Critical regulation of voltages supplied to the flicker-rate generator and light source.

3. Frequent check measurements of the level of the flicker light source and of that of the background illumination.

4. A light source of size, intensity, field uniformity, and other physical properties consonant with optimal perception of critical fusion value in view of the recommendations in the available literature.

5. An automatically regulated frequency sweep at a rate designed to minimize reaction time errors.

6. Control by a stop-switch in the hands of the subjects.

7. Performance of the test through standard monocular artificial pupillary apertures or through binocular lenses compensating for the critical fusion value divergence between the two eyes in order to eliminate pupillary factors in evaluating results.

The possible cost of such equipment and the equivocal results obtained in clinical applications to date would seem to suggest that work along these lines might best be restricted to research facilities for the present. Among the major problems for attention should be reliable reproducibility of results from worker to worker and a concentrated effort toward increased accuracy, consistency, and agreement on the meaning and causation of specific changes.

In view of all these factors and others not yet clearly apparent, it is felt that much more work of a basic nature needs to be done before variations in critical fusion value under the influence of nitroglycerin or other drugs may be reliably applied in

clinical evaluations of medical conditions such as hypertension.

#### SUMMARY

1. The nitroglycerin flicker-fusion technique, modified for greater precision, using the Krasno-Ivy flicker photometer, has been tested upon 51 normotensive and 46 hypertensive individuals.

2. In this series, neither hypertensive nor normal groups responded with the uniformity anticipated from the original description of the test.

3. Statistical analysis of this material appears to validate these data.

4. A review has been presented of many pertinent physical and physiologic properties which must be considered in the application and interpretation of the test.

5. Attempts to demonstrate measurable retinal vascular changes following nitroglycerin administration have not been successful by ophthalmoscopy or retinal photography.

6. Changes in pupil size have been presented which may occur even in the absence of nitroglycerin and may thus induce or interfere with critical fusion value changes or mask by compensation other possible critical fusion value changes in the course of the test.

7. Criteria have been presented for more uniform and reliable instrumentation.

*University Hospital (1)*

*706 Garden Oaks Boulevard (18).*

#### ACKNOWLEDGEMENT

The authors acknowledge with gratitude the helpful criticism of Dr. Robert D. Taylor and Dr. Irvine H. Page. We wish also to thank Miss Ruth Meier for her technical assistance in the statistical analysis and Mr. Tom Lannon and Mr. Kurt Smolen of the Department of Photography of the Cleveland Clinic for preparation of the photographs.

#### REFERENCES

1.(a) Hines, E. A., Jr., and Brown, G. E.: A standard stimulus for measuring vasomotor reactions: Its application in the study of hypertension. *Proc. Staff Meet. Mayo Clin.*, 7:332, 1932.

(b) ———: A standard test for measuring the variability of blood pressure: Its significance as an index of the prehypertensive state. *Ann. Int. Med.*, 7:209, 1933.

2. Spankus, W., Page, I. H., and Corcoran, A. E.: Personal communication.



3. Enzer, N., Simonson, E., and Blankstein, S. S.: Fatigue of patients with circulatory insufficiency investigated by means of the fusion frequency of flicker. *Ann. Int. Med.*, **16**:701, 1942.
4. Simonson, E., and Enzer, N.: Measurement of fusion frequency of flicker as a test for fatigue of the central nervous system: Observations of laboratory technicians and office workers. *J. Indust. Hyg. & Toxicol.*, **23**:83, 1941.
5. Simonson, E., Enzer, N., and Blankstein, S. S.: Effect of amphetamine (Benzedrine) on fatigue of the central nervous system. *War Med.*, **1**:690, 1941.
6. Simonson, E., and Enzer, N.: Effect of Pervitin (desoxyephedrine) on fatigue of the central nervous system. *J. Indust. Hyg. & Toxicol.*, **24**:205, 1942.
7. Krasno, L. R., and Ivy, A. C.: The response of the flicker fusion threshold to nitroglycerin and its potential value in the diagnosis, prognosis, and therapy of subclinical and clinical cardiovascular disease. *Circulation*, **1**:1267, 1950.
8. Sloan, L. L.: Instruments and technics for the clinical testing of light: IV. Size of pupil as a variable factor in the determination of the light minimum. *Arch. Ophthalm.*, **24**:258, 1940.
9. Speiser, S.: Ueber die Beeinflussung der kritischen Flimmerfrequenz durch verschieden weite Pupillen. *Ophthalmologica*, **116**:357, 1948.
10. Miles, P. W.: Flicker fusion frequency in amblyopia ex anopsia. *Am. J. Ophthalm.*, **32**:225 (June, Pt. 2) 1949.
11. ———: Flicker fusion fields: I. The effect of age and pupil size. *Am. J. Ophthalm.*, **33**:769, 1950.
12. Granit, R., and Harper, P.: Comparative studies on the peripheral and central retina: II. Synaptic reactions in the eye. *Am. J. Physiol.*, **95**:211, 1930.
13. Cobb, P. W.: The effect on foveal vision of bright surroundings. *J. Exper. Psychol.*, **6**:540, 1916.
14. ———: The dependence of flicker on the dark-light ratio of the stimulus cycle. *J. Optic. Soc. America*, **24**:107, 1934.
15. Crozier, W. J., Wolf, E., and Zerhorn-Worl, G.: Intensity and critical frequency for visual flicker. *J. Gen. Physiol.*, **21**:203, 1938.
16. Hecht, S., et al.: The visual functions of the complete color-blind. *J. Gen. Physiol.*, **31**:459, 1948.
17. Willmer, E. N.: *Retinal Structure and Colour Vision: A Restatement and an Hypothesis*. London, Cambridge Univ. Press, 1946, p. 151.
18. Miles, P. W.: Flicker fusion fields: II. Technique and interpretations. *Am. J. Ophthalm.*, **33**:1069, 1950.
19. ———: Personal communications, 1950.
20. Phillips, G.: Perception of flicker in lesions of the visual pathways. *Brain*, **56**:464, 1933.
21. Wald, G., and Burian, H. M.: The dissociation of form vision and light perception in strabismic amblyopia. *Am. J. Ophthalm.*, **27**:950, 1944.
22. Tyler, D. B.: The fatigue of prolonged wakefulness. *Federation Proc.*, **6**:218, 1947.
23. Brozek, J., and Keys, J.: Flicker fusion frequency as a test of fatigue. *J. Indust. Hyg. & Toxicol.*, **26**:169, 1944.
24. Enzer, N., Simonson, E., and Blankstein, S. S.: The reappearance of flicker at high flash frequency in patients with brain pathology and in normal subjects. *J. Lab. & Clin. Med.*, **29**:63, 1944.
25. Larson, P. S., Finnegan, J. K., and Haag, H. B.: Observations on the effect of cigarette smoking on the fusion frequency of flicker. *J. Clin. Investigation*, **29**:483, 1950.
26. Tanner, W. P.: A preliminary investigation of the relationship between visual fusion of intermittent light and intelligence. *Science*, **112**:201, 1950.
27. Fertig, H., Corcoran, A. C., and Page, I. H.: Unpublished data.
28. Lythgoe, R. J., and Tansley, K.: *The adaptation of the eye: Its relation to the critical fusion frequency of flicker*. London, His Majesty's Stationery Office, 1929. (Med. Res. Council Special Report Series No. 134.)
29. Kravkov, S. V.: Critical frequency of flicker and indirect stimuli, *C. R. Acad. Sc. U.R.S.S.*, **22**:64, 1939.
30. Page, I. H., and Corcoran, A. C.: *Arterial Hypertension: Its Diagnosis and Treatment*. Chicago, Year Book Publishers, 1949, ed. 2.
31. Weiss, S., and Ellis, L. B.: Influence of sodium nitrite on the cardiovascular system and on renal activity in health, in arterial hypertension, and in renal disease. *Arch. Int. Med.*, **52**:105, 1933.
32. Wilkins, R. W., Weiss, S., and Haynes, F. W.: The effect of epinephrin in circulatory collapse induced by sodium nitrite. *J. Clin. Investigation*, **17**:41, 1938.
33. Gellhorn, E., Darrow, C. W., and Yesnick, L.: Effect of epinephrine on convulsions. *Arch. Neurol. & Psychiat.*, **42**:826, 1939.
34. Keith, N., Wagener, H. P., and Kernohan, J. W.: The syndrome of malignant hypertension. *Arch. Int. Med.*, **41**:141, 1928.
35. Granit, R.: Personal communication.
36. Donders, F. C.: On the anomalies of accommodation and refraction of the eyes. (Tr. by W. D. Moore.) London, New Sydenham Society, 1864, p. 573.
37. Duke-Elder, W. S.: *Textbook of Ophthalmology*. London, Kimpton, 1932. v. 1, p. 753.

39. Hoorens, A.: Influences de l'asphyxie, de l'anemie, de l'hypoxemie et du CO<sub>2</sub> sur la pupille. Arch. Internat. pharmacodyn., **77**:464, 1948.
40. Ward, A. A., Jr., and Reed, H. L.: Mechanism of pupillary dilatation elicited by cortical stimulation. J. Neurophysiol., **9**:329, 1946.
41. Spring, K. H., and Stiles, W. S.: Variation of pupil size with change in angle at which light stimulus strikes retina. Brit. J. Ophth., **32**:340, 1948.
42. Gellhorn, E., Darrow, C. S., and Yesinick, L.: Effect of variation of blood pressure on the autonomic nervous system. Proc. Soc. Exper. Biol. & Med., **43**:236, 1940.
43. Hirschfelder, A. D.: Effects of drugs upon the vessels of the pia mater and retina. J. Pharmacol. & Exper. Therap., **6**:597, 1915.
44. Hylkema, B. S.: Fusion frequency with intermittent lights under various circumstances. Acta Ophth., **20**:159, 1942.

## THE CATARACT OPERATION AS AN OFFICE PROCEDURE

LYNDON EVELYN, LRCP LOND., MRCS ENG.

*Kingston, Jamaica, B.W.I.*

Different countries face different conditions and customs. Here in Jamaica, as elsewhere in the tropics, there is a great deal of poverty. This imposes on government and voluntary social organizations a real limit as to what can be done to help those who need hospitalization for operative purposes.

It seemed to me that long hospital waiting lists could be reduced and workers could be returned to their labors in shorter time if the cataract operation were done in my consulting rooms and the patients sent home for convalescence.

This is a preliminary note on only seven cases but, as all have been completely successful, it is hoped that others will experiment with the procedure and, no doubt, improve upon it. It definitely works and might be found to have its uses in hospital eye clinics, which are invariably large in the tropics. A technique of selection of most suitable cases will no doubt soon be found.

The start in doing operations at the office was made in 1948 with dissections of tonsils under local anesthetic. Intranasal antrostomies and needlings followed along with surgery on lacrimal sacs, pterygia, and cysts. Shortly after this iridectomies were done and then excision of eyes. Later on iridencleisis was performed and I felt that the radical antrum operation could also be done.

Even at this stage, however, I did not

have in mind the cataract operation, and it was not until after a visit to the United States in 1951, when I was able to see and study the latest methods of intracapsular extraction, that the idea gradually formed in my mind. Arrangements were made, but it was not easy to find a suitable patient to start with. However, the first cataract operation was done on February 10, 1953.

Out of a total of 970 ear, nose, throat, and eye operations of all types (but not including foreign bodies in the cornea, pterygia, or cysts) done over a period of six years, two cases have been lost. One was of a foreign body embedded in the cornea of an eye which, after removal, ulcerated. Eventually the eye became infected and had to be removed in the office. The second was a case of pterygium overtaken by the same fate. The eye was removed in the Kingston Hospital.

The office facilities include an operating room with proper lighting, complete and adequate sterilization, and high-grade instruments. A competent staff nurse has made these operations not only possible but successful. The only other assistant is an office maid to answer the telephone and so forth.

The patient to be operated on, having been checked for blood pressure, urine, dental and nasal sepsis, is told to take a mild purgative to produce one, and not more than

two, evacuations on the morning of the operation. The patients are also given Noc-tinal\* (3.0 gr.) the night before the operation in order to ensure a good night's rest. On the morning of the operation, they are permitted tea at about five-thirty, and present themselves at the office with a friend or relative at about seven o'clock.

Noctinal (1.5 to 3.0 gr.), with or without Demerol or morphine ( $\frac{1}{8}$  to  $\frac{1}{4}$  gr.), depending on the degree of relaxation of the patient as judged by the neck muscles, is administered. While the patient is relaxing on the table, the instruments are sterilized and 400,000 units of procaine penicillin G and 10 mg. of vitamin K are given. The penicillin and vitamin K are repeated for the three successive days following the operation. The operation is commenced between eight-thirty and nine o'clock.

Anesthesia is by means of 15 cc. of Novutox† in and around the orbicularis muscle above and below the eye, and one cc. of Novutox as a retrobulbar injection. Slight pressure is immediately placed on the eye after the retrobulbar injection in the hope of preventing a sometimes troublesome retro-ocular hemorrhage. Cocaine hydrochloride (4.0 percent) and neosynephrine (10 percent) are also instilled into the eye to ensure complete anesthesia and a fully dilated pupil. Argyrol (25 percent) is then instilled to precipitate the proteins. The lacrimal sac is then washed through, first with normal saline, and after with a 10-percent solution of crystalline penicillin drops. Sterile towels are then applied and retraction is obtained by means of the mosquito clamps of Castroviejo. A bridle suture is put through the superior rectus tendon and the eye is ready for commencing the operation.

The section of the cornea is started by means of a keratome and completed with the

corneal scissors of Castroviejo. Complete hemostasis of all the scleral and conjunctival vessels is obtained with a small metallic bead heated in a spirit lamp. This is of the utmost importance. Three corneoscleral sutures are inserted and a peripheral iridectomy performed.

The lens is then dislocated and the anterior capsule is grasped, with the cross-action forceps of Castroviejo, in its upper part. The lens is removed in capsule, using the Kirby technique; however, the remainder of the technique is that of Castroviejo.

After the lens is removed, the corneo-scleral sutures are drawn and tied, and the complete conjunctiva is sutured at two-mm. intervals. Air is instilled into the anterior chamber. The operation is now complete. Penicillin drops are instilled together with physostigmine and sulfathiazole ointment. A Ring's mask is applied over a light fluffed-up gauze dressing. The Ring's mask is then cut out over the nonoperated eye so the patient can use it.

The patients are then sent home and told to remain in bed for the rest of that day. They are, however, allowed to move about in bed as freely as they please and are on full diet. If necessary, an occasional cigarette is allowed and also alcohol. In other words, the patient is encouraged to get back on his feet as soon as possible, and stooping and straining are the only don'ts. The second day is spent at home.

On the third day the patient returns to the office; the eye is dressed and atropine drops and ointment are instilled. He returns to the office for dressing every other day for the first week. During the second week, he returns every third day. At the end of 14 days the stitches are removed at the office. As a rule only the three deep sutures need to be removed at this time, the others having fallen or sloughed out.

The Ring's mask is worn for the week following the removal of the stitches, after which the patient is given dark glasses with side pieces for protection. These are worn

\*A barbiturate manufactured by Charles E. Frosst & Co., Montreal.

†A local anesthetic made by the Pharmaceutical Manufacturing Company, Ashley Road, Epsom, Surrey.

for a varying period. Cataract glasses are prescribed as soon as the patient can take them but at least two months after the date of operation.

So far the results have been very encouraging; however, I must stress again that I do not advocate this method as a general procedure. I wish only to point to what can be done. Arguments against this method would consider the chief complications of (1) hemorrhage, (2) sepsis, and (3) detachment of the retina. Hemorrhage can occur, in fact all three complications can occur, in patients treated in institutions; as a rule, the hemorrhage will clear up. Sepsis usually can be combatted with antibiotics but now and again infections will occur. Detachment has not occurred in this small series of cases. If it should occur, the patient should, of course, be hospitalized and the necessary operation performed.

#### CASE REPORTS

##### CASE 1

Mrs. L. J., aged 63 years, was seen on February 2, 1953. Vision was: R.E., counting fingers; L.E., hand movements. Blood pressure was 170/115 mm. Hg. The urine showed a trace of sugar. No sepsis was present.

On February 10, 1953, operation was performed as an office procedure. Blood pressure was 200/130 mm. Hg, so one pint of blood was drawn. Noctinal (1.5 gr.) and morphine sulfate (1/6 gr.) were given. An intracapsular extraction was done on the left eye.

She was discharged on May 4, 1954, with vision of the left eye: Snellen, 6/9 and J1, with a +11.0D. sph.  $\ominus$  +1.5D. cyl. ax. 90°, add +4.0D. sph. for near.

##### CASE 2

Mrs. M. I., aged 64 years, was unable to see when examined on April 9, 1953, vision, O.U., being finger counting only. Blood pressure was 150/70 mm. Hg. Urine showed a slight trace of sugar. No sepsis was

present. Both eyes showed chronic glaucoma (35 mm. Hg [Schiotz]). Because of the cataracts, the discs could not be seen.

On April 16, 1953, as an office procedure, an intracapsular extraction with wide iridectomy was performed on the left eye. The intraocular hemorrhage which followed cleared after three months to reveal marked cupping of the disc.

On February 19, 1954, vision in the left eye was counting fingers (not improved) and there was no central field. The eye was quiet. Tension was 30 mm. Hg (Schiotz).

In this case, cataract extraction was successful and the glaucoma was benefited by the wide iridectomy but the vision was not improved.

##### CASE 3

Mrs. M. L., aged 60 years, was seen on July 7, 1953, having been referred by Dr. D. K. Weston as a case suitable for office cataract extraction.

Vision was perception of light, O.U. Blood pressure was 180/105 mm. Hg. Urine was negative and no sepsis was present.

An intracapsular extraction was performed on the right eye on July 22, 1953. On March 27, 1954, vision in the right eye was Snellen 6/18 and J4 with a +11.0D. sph.  $\ominus$  +1.0D. cyl. ax. 90°, add +4.0D. sph. for near.

This patient developed a small central patch of keratitis which no treatment would help and which is the cause of her poor vision.

##### CASE 4

Mrs. I. S., aged 58 years, was first examined on September 1, 1953, because she was unable to see with her left eye which had suffered a blow about one year ago. Vision was: R.E. 6/12; L.E., light perception. Blood pressure and urine were normal. There was no septic condition.

On September 17, 1953, an extracapsular extraction on the left eye was performed as an office procedure. Remnants of capsule

were removed with capsule forceps and by irrigation.

On February 2, 1954, vision in the left eye was Snellen 6/9 and J2, with a +8.0D. sph.  $\ominus$  +2.0D. cyl. ax. 135°, add +4.0D. sph. for near.

#### CASE 5

Mr. A. L., aged 27 years, was seen on September 1, 1952, because of a blind right eye, present for years. Vision was: R.E., light perception; L.E., 6/6. There was a traumatic cataract of the right eye. Blood pressure and urine were normal. He had infected tonsils.

On September 29, 1953, under local anesthesia, the tonsils were dissected at the office.

On October 15, 1953, an extracapsular extraction of the cataract on the right eye was performed as an office procedure. The remnants of capsule were removed with capsule forceps.

On November 28, 1953, vision in the right eye was Snellen 6/9 and J1 with a +11.0D. sph.  $\ominus$  +1.0D. cyl. ax. 180°, add +4.0D. sph. for near.

#### CASE 6

Mr. R. A. S., aged 68 years, was seen on November 10, 1953. Vision was: R.E., 6/18;

L.E., light perception. Blood pressure and urine were normal. There was no sepsis. There were bilateral cataracts, the one of the left eye being mature.

On January 27, 1954, an intracapsular extraction was performed on the left eye as an office procedure. On April 23, 1954, vision in the left eye was 6/6 with a +10.0D. sph.  $\ominus$  +1.5D. cyl. ax. 90°, and J1 with a +4.5D. sph. for near.

#### CASE 7

Mrs. V. J., aged 50 years, was seen on December 2, 1953, with vision, O.U., counting fingers. There were bilateral cataracts. Blood pressure and urine were normal. There was no sepsis.

On February 3, 1954, at the office, an intracapsular extraction was done on the left eye. On February 6th, severe pain developed in the operated eye. On February 8th, tension was elevated and there was hemorrhage in the anterior chamber. She was treated with pilocarpine and DFP, and the next day (February 9th) showed improvement. By February 16th, the eye was clear and the tension soft.

On April 3, 1954, vision in the left eye was 6/12 with a +10.0D. sph.  $\ominus$  +2.5D. cyl. ax. 60°, and J2 with a plus 5.0D. sph. for near.  
75 Church Street.



## OBJECTIVE METHODS OF REFRACTION\*

### A COMPARISON OF THE RODENSTOCK EYE-REFRACTOMETER AND THE REID STREAK-RETINOSCOPE IN DETERMINING THE REFRACTIVE STATUS OF AN EYE

DAVID VOLK, M.D.

*Cleveland, Ohio*

The recent emphasis placed upon the Rodenstock Eye-Refractometer as an objective means of determining the refractive status of an eye has prompted me to attempt an evaluation of this instrument and to compare it with a retinoscope.

The refractometer, similar in principle to lens measuring instruments such as the lensometer, is so constructed that an image of a test plate can be made to diverge from a point in front of the eye or converge toward a point behind the eye being examined.

When accommodation is relaxed, it is possible to direct the test-plate image at the far point of the eye and thus obtain a clear image of it upon the retina. If accommodation is not relaxed, it is still possible to obtain a clear image upon the retina, provided the test-plate image is placed at the point for which the eye is accommodated. The adjustment necessary to produce a clear image on the retina is calibrated in terms of diopters of correcting lens placed in the spectacle plane of the eye.

In cases of astigmatism, the far point for each of the principal meridians is located. The examiner must observe the retinal image through a telescope placed in front of the examined eye, the telescope being automatically adjusted to produce clear imagery when the test-plate image is sharply focused on the retina of the subject.

In order to relax accommodation the instrument is set at more plus or less minus

than the refractive error and then the instrument is adjusted to produce a clear retinal image in the first principal meridian. The test plate must be rotated during this procedure so as to locate the principal meridians.

The refractive status in the first principal meridian having been determined, the instrument is adjusted in the minus direction until the part of the image on the retina corresponding to the second principal meridian appears clear. The difference between the two readings is the astigmatic correction in terms of minus cylinder. The first reading is the spherical correction.

The retinoscope used throughout the experiment was a Reid-streak. A trial frame was used and retinoscopy was performed with spheres and minus cylinders.

#### EXPERIMENTAL PROCEDURE

Each patient was tested with the retinoscope and the refractometer, and examined subjectively. For the subjective examination, either the retinoscope or the refractometer findings would be placed in a trial frame and spheres and minus cylinders would be varied until maximum visual acuity was obtained on the Snellen chart.

The spheres were varied in steps, at times as low as one-eighth diopter, as were the cylinders, the power and axis of the cylinders being changed as indicated by a  $+0.25$ ,  $-25$ -diopter cross cylinder.

The criteria for the subjective spherical correction was that the most plus lens or least minus lens which enabled maximum visual acuity was correct. The cylinder was considered correct for both power and axis when reversals of the cross-cylinder for both power and axis resulted in the same amount

\*From the Western Reserve University School of Medicine and the Department of Surgery, Ophthalmological Service, of the University Hospitals of Cleveland.

of blur for the smallest readable line of letters for either position of the cross-cylinder. Any change in cylinder, either in power or axis, was followed by a recheck of the sphere, and this in turn followed by a recheck in the cylinder. This procedure was continued until the desired end-point was reached.

The retinoscope and the refractometer were alternately used as the first instrument with consecutive patients. A record of the time required for use of the refractometer and for the retinoscope was recorded in many instances. All examinations were performed by me.

#### SUBJECT MATERIAL

The patients serving as subjects for the experiment were an unselected group of clinic patients at the refraction clinic of University Hospital of Cleveland. The data for the tables, graph, and statistical analyses were obtained from a total of 32 patients.

From these 32 patients there were 37 eyes examined under homatropine and 52 eyes examined without cycloplegia. Of the 52 eyes, 28 had been examined previously under homatropine and were included as part of the group of 37.

In the 89 single-eye examinations, subjectively corrected visual acuity was 20/20

TABLE 1

AGE DISTRIBUTION OF THE 32 PATIENTS FROM WHOM THE DATA WAS OBTAINED FOR THE STATISTICAL ANALYSIS

Ages (yr.)	Number of Patients
11 to 15	5
16 20	5
21 25	2
26 30	1
31 35	3
36 40	4
41 45	3
46 50	2
51 55	0
56 60	1
61 65	1
66 70	2
71 75	2
76 80	1

TABLE 2\*

DISTRIBUTION OF THE SPHERICAL PORTION OF THE SUBJECTIVE CORRECTION FOR THE 89 SINGLE-EYE EXAMINATIONS

Spherical Portion of Subjective Correction (diopters)	Number of Eyes
-7.00	4
-4.75	1
-4.50	2
-4.25	0
-4.00	3
-3.75	0
-3.50	0
-3.25	1
-3.00	2
-2.75	5
-2.50	2
-2.25	2
-2.00	1
-1.75	3
-1.50	3
-1.25	4
-1.00	2
-0.75	4
-0.50	2
-0.25	4
0.00	4
+0.25	4
+0.50	6
+0.75	6
+1.00	5
+1.25	4
+1.50	5
+1.75	0
+2.00	3
+2.25	1
+2.50	0
+2.75	1
+3.00	1
+3.25	0
+3.50	0
+3.75	0
+4.00	0
+4.25	0
+4.50	0
+4.75	1
+5.00	2
+7.50	1

\* The 52 noncycloplegic examinations and the 37 homatropine examinations are included. Spheres falling in the 0.12 diopter intervals have been placed in the 0.25 diopter groupings in this table.

or better in 77 instances, 20/25 in seven instances, 20/30 once, 20/40 once, 20/50 once, and 20/70 twice.

The age distribution of the 32 patients, ranging from 11 to 77 years, is shown in Table 1. The distribution of the spherical component of the subjective corrections for the 89 eyes is shown in Table 2. The dis-

TABLE 3

DISTRIBUTION OF THE SUBJECTIVE ASTIGMATISM CORRECTIONS FOR THE 89 EYES

Minus Cylinder Correction	Number of Eyes
(diopters)	
0.00	8
-0.12	1
-0.25	14
-0.37	12
-0.50	11
-0.62	2
-0.75	8
-0.87	2
-1.00	9
-1.12	1
-1.25	9
-1.50	3
-1.75	3
-2.00	1
-2.25	1
-2.50	1
-2.75	1
-3.00	2

tribution of the subjective astigmatic corrections for the 89 eyes is shown in Table 3.

In addition to these 89 eyes, six aphakic eyes and three eyes showing some unusual circumstances were studied; however, they are not included in the statistical analysis.

#### CRITERIA FOR ANALYSIS OF DATA

Throughout this paper the subjective correction is considered the correct answer, any difference between the objective method and the subjective method being considered an error for the objective method. For example, if in a particular case the refractometer indicates a correction of +0.25 diopters, the retinoscope indicates a correction of +1.50 diopters, and the subjective correction is +1.00 diopters, then the refractometer is in error -0.75 diopters and the retinoscope is in error +0.50 diopters.

For cylinders, failure to find as much cylinder objectively as is found subjectively is considered a plus error, while finding more cylinder objectively than is found subjectively is considered a minus error. When the axis of the cylinder as found objectively is more than 45 degrees from the axis of the cylinder as found subjectively, the error

is considered a plus error equal in amount to the sum of the objective and the subjective cylinders.

The data may also be analyzed by averaging the errors for the instruments without regard to the sign of the error. This procedure will not indicate the trend of the errors, that is, whether the errors tend to lie toward the plus or minus side, but it does indicate the average amount by which the instrument fails to indicate the subjective correction. Such an analysis has been done and is presented in tabular form as the average error, along with other results, in Table 6, which summarizes the results of all the data.

#### RESULTS

The trend of the general refractive status of the 52 noncycloplegic eyes was determined for each of the three methods of examination. Only the spherical components of the corrections was used in the computations.\* The mean of all corrections for the subjective method was -0.03 diopters. For the retinoscope the mean correction was -0.05 diopters, and for the refractometer the mean correction was -0.64 diopters. These values indicate a relatively large shift of the distribution toward the minus side for the refractometer, in contrast to the retinoscope which shows a very small shift, when compared to the subjective method.

The mean error of the refractometer for the spherical components of the 52 noncycloplegic eyes was found to be -0.61 diopters with a standard deviation of 0.86. These same eyes as measured with the retinoscope

\* Experimental evidence (to be published) which I have obtained during another study shows that in almost all cases the circle of least confusion does not provide maximum visual acuity in uncorrected astigmatism. Maximum acuity occurs in most cases when a focal line is on or near the retina, the particular focal line being specific for each eye. Since the theoretic concept of the spherical equivalent has not been borne out by my studies, I preferred to use the spherical component in the computations, rather than the spherical equivalent.

showed a mean error of  $-0.02$  diopters and a standard deviation of  $0.31$ . The critical ratio of the difference between the two standard deviations is  $6.1$ , indicating that this difference is highly significant and could not have occurred by chance.

As for the cylindric errors for the 52 eyes, with the refractometer there were 22 instances in which no cylinder was found when one was found by the subjective method with values up to  $1.25$  diopters not being found. There were three instances in which the axis differed by more than  $45$  degrees from the subjective axis.

With the retinoscope there were six instances of failure to find the cylinder found subjectively, with the subjective values of those cylinders not found not exceeding  $0.50$  diopters. In one eye a cylinder was found by retinoscopy but not subjectively, and there was one instance of an error in axis of more than  $45$  degrees.

The mean error and standard deviation of the cylindric corrections for these 52 eyes as measured with the refractometer are  $+0.23$  and  $0.59$ , respectively. With the retinoscope the corresponding values are  $+0.08$  diopters and  $0.38$ . The critical ratio of the difference between the standard deviations is  $3.18$ , also indicating a high significance of the differences obtained by the two methods of measurement.

The average error in cylinder axis as determined with the refractometer was  $16.4$  degrees in contrast to an average error of  $9.8$  degrees for the retinoscope.

For the 37 eyes examined under homatropine, the mean spherical error and standard deviation was found to be  $-0.36$  diopters and  $0.47$ , respectively, with the refractometer. With the retinoscope the mean spherical error and standard deviation was found to be  $-0.19$  diopters and  $0.37$ , respectively. The critical ratio of the difference between the standard deviations is  $1.45$ , indicating that much less significance can be placed upon the differences obtained.

For the cylinders in these eyes, with the

refractometer the mean error was  $+0.18$  diopters with a standard deviation of  $0.45$ . For the retinoscope the mean error was  $+0.06$  diopters with a standard deviation of  $0.31$ . The critical ratio for these values is  $2.22$ , indicating a fairly significant difference.

With the refractometer there were 12 instances of failure to find a cylinder when one was found subjectively, all cylinders being  $0.50$  diopters or less. There were also two instances in which a cylinder was found with the refractometer when there was none subjectively. There were also two instances in which the error in axis exceeded  $45$  degrees. The average error of the axis in those cases in which cylinders were found with the refractometer and subjectively was  $17.8$  degrees.

With the retinoscope there were eight instances of failure to find a cylinder when one was found subjectively, the values of the subjective cylinders not exceeding  $0.75$  diopters. There were two instances in which a cylinder was found with the retinoscope when none was found subjectively. The difference in axis in those cases in which a cylinder was found by both retinoscopy and subjectively did not exceed  $25$  degrees, with an average error of five degrees.

For 28 patients, the time required for the examination of both eyes with the refractometer was recorded, resulting in a mean time of  $4.2$  minutes. The measurement of time began after the patient was seated at the instrument with his head in the proper position, and was ended as the final readings were obtained. Time was measured to the nearest one-half minute. With the retinoscope for a series of 20 patients, the mean time was  $3.7$  minutes. The measurement of time began after the trial frame had been properly placed upon the patient's face.

In the six aphakic eyes, the refractometer examination was generally difficult to perform. The retinal image in one instance was so blurred, reduplicated, and poorly seen that the examiner was uncertain of the end-point.

TABLE 4  
ERRORS FOR SIX APHAKIC EYES

Spheres		Cylinders		Axis	
Refractometer	Retinoscope	Refractometer	Retinoscope	Refractometer	Retinoscope
(diopters)	(diopters)	(diopters)	(diopters)	(degrees)	(degrees)
+3.50	+1.50	-2.00	-2.00	0	0
-0.25	+0.75	+0.75	0.00	10	0
+0.50	-0.50	+4.00	+0.50	No cyl. found	5
+2.00	0.00	-2.00	-1.50	0	10
-1.50	0.00	-0.50	-0.50	13	0
-2.00	0.00	+1.25	-1.25	12	10

The error in the sphere for this case was  $-2.00$  diopters and for the cylinder  $+1.25$  diopters. With retinoscopy there was no error in the sphere and a  $-1.25$  diopter error in the cylinder. In another aphakic eye in which the media were quite hazy, the examiner failed to find a four-diopter cylinder with the refractometer. The cylinder was easily found with the retinoscope with an error of  $+0.50$  diopters.

The errors for the six aphakic eyes have been tabulated in Table 4.

In two eyes with immature cataracts and macular degeneration, retinoscopy was performed quite accurately although with difficulty. The refractometer examination could not be done on these eyes as a result of the inability of the examiner to see the retinal image. In an eye with diabetic retinopathy and vitreous opacities, the examination could not be performed with the refractometer but was done accurately although with difficulty with the retinoscope.

### DISCUSSION

Examination of the results shows that statistically the retinoscope is more accurate than the refractometer. The differences between the means and the standard deviations obtained by the two methods are highly significant with the exception of the homotropine spheres. Here the critical ratio of the difference between the standard deviations indicates that the differences obtained by the two methods might not be statistically significant and could have occurred by chance.

In the noncycloplegic series of eyes the results show the refractometer to be much less accurate than the retinoscope. The mean error of  $-0.61$  diopters and the quite large standard deviation of  $0.86$  for the refractometer-determined spheres indicate that some of the patients had been accommodating. This can readily be seen by inspection of Figure 1 which presents graphically the errors in the spheres for the refractometer and the retinoscope for the 52 noncycloplegic eyes.

Further evidence that this is the case is the smaller mean error,  $-0.36$  diopters, and the smaller standard deviation,  $0.47$ , obtained with the refractometer in the homotropinized series of eyes, in which case some, if not all, accommodation has been eliminated. The reduction in the spread of errors as well as the shift of the distribution of errors toward the zero point when homotropine is used is accounted for by its effect upon accommodation.

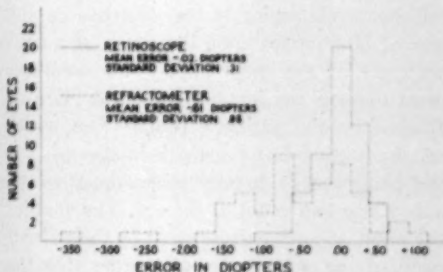


Fig. 1 (Volk). Distribution of errors in the spherical portion of the correction for the 52 eyes examined, without cycloplegia, by the retinoscope and by the refractometer.



The critical ratio of the difference between the standard deviations for the homotropinized series of eyes versus the noncycloplegic series of eyes which were examined with the refractometer is 3.9. This value is highly significant and indicates that the difference could not have occurred by chance.

A patient being examined with the refractometer probably develops some conception of nearness of the test-plate image which he fixates, the amount of accommodation varying for different subjects. A preconceived notion of nearness of the test-plate image could very well occur in a patient who observes the refractometer prior to his being tested. He is asked to fixate a target which he knows is in the apparatus and not at a great distance. Forcing relaxation of accommodation by setting the instrument at a more plus or less minus position than is expected does not result in complete relaxation, as is indicated by the data.

The raw data for the spherical portion of the correction for the 52 noncycloplegic eyes are presented in Table 5 for the three methods of examination. Inspection of these data shows that, when accommodation does occur with the refractometer, it very often does so for both eyes of a pair. This may be taken as additional evidence that true accommodation does occur with the refractometer.

Another factor which may account for the larger spread of spherical and cylindric errors with the refractometer when used without cycloplegics is the decrease in the size of blur circles upon the retina as a consequence of the small pupil. The examiner must observe the image of the test plate as formed on the patient's retina. The width of the out-of-focus retinal image of the test-plate lines is directly proportional to the size of the exit pupil of the eye. The smaller the pupil, the more gross must be the adjustment of the refractometer in order that the examiner be able to observe a change in the sharpness of the retinal image, with the result that accuracy will be decreased.

A smaller pupil also tends to decrease the brightness of the retinal image, another factor which may make the determination of the adjustment which produces the sharpest retinal image a more difficult task.

In many instances the retinal image could never be made to appear distinct regardless of the adjustment of the instrument, the image in one meridian generally appearing more blurred than in the other. This must be attributed to the aberrations of the eye, disturbed medias, and irregular astigmatism, the effect of these factors generally being increased with a mydriatic or cycloplegic. After several attempts to produce a clear image, the examiner would have to choose what he thought was the least blurred image as the end-point.

Since the examiner is observing a target which is essentially a pair of crossed lines, his own astigmatism, if uncorrected, might cause one or the other of the lines to appear blurred even though both lines were clearly focused on the subject's retina. Furthermore, the image which the examiner must observe is quite small and demands good acuity on the part of the examiner.

A moderate degree of disturbed vision in the examiner will not prevent him from performing accurate retinoscopy but will interfere with accurate end-point determination with the refractometer. Slight movements of the patient's head or eyes may make the brightness and sharpness of the retinal image vary greatly.

All the factors mentioned, and others, tend to make the refractometer a more difficult and less accurate instrument to use in comparison with the retinoscope. With the retinoscope, accommodation can very easily be controlled by having the patient look at a distant point while retinoscopy is being performed.

When cycloplegics and mydriatics are being used, the effect of aberrations upon retinoscopy can be partially eliminated by disregarding the periphery and neutralizing the central part of the reflex. It should be

TABLE 5

SPHERICAL PORTION OF THE CORRECTING LENS FOUND BY EACH OF THE METHODS  
OF EXAMINATION FOR THE 52 NONCYCLOPLEGIC EYES

Subjective Sphere	Retinoscope Sphere	Retinoscope Error	Refractometer Sphere	Refractometer Error
(diopter)	(diopter)	(diopter)	(diopter)	(diopter)
+0.50	+0.50	0.00	-1.00	-1.50
+0.75	+1.25	+0.50	0.00	-0.75
-2.25	-2.50	-0.25	-2.00	+0.25
-1.75	-2.25	-0.50	-2.25	-0.50
-3.25	-3.00	+0.25	-3.00	+0.25
-3.00	-3.00	0.00	-4.00	-1.00
+1.00	+1.00	0.00	+1.00	0.00
+1.00	+1.25	+0.25	+1.00	0.00
+2.00	+2.50	+0.50	+2.00	0.00
+2.25	+2.75	+0.50	+1.00	-1.25
+1.00	+0.75	-0.25	+0.50	-0.50
+0.75	-0.25	-1.00	+0.50	-0.25
+0.50	+0.25	-0.25	-0.25	-0.75
-1.75	-2.00	-0.25	-3.25	-1.50
-1.75	-1.75	0.00	-3.00	-1.25
+0.25	+0.50	+0.25	-0.50	-0.75
+0.50	+0.50	0.00	-1.25	-1.75
0.00	+0.25	+0.25	-3.50	-3.50
0.00	+0.25	+0.25	-2.50	-2.50
+2.75	+2.50	-0.25	+3.50	+0.75
+3.00	+2.50	-0.50	+3.75	+0.75
-0.50	-0.25	+0.25	-0.50	0.00
-0.25	0.00	+0.25	-1.50	-1.25
-0.87	-0.75	+0.12	-1.75	-0.87
-0.75	-0.75	0.00	-1.75	-1.00
+1.00	+1.00	0.00	+0.75	-0.25
+1.25	+1.25	0.00	+1.25	0.00
-1.37	-1.25	+0.12	-1.75	-0.37
-1.00	-0.75	+0.25	-1.25	-0.25
-4.75	-4.50	+0.25	-6.00	-1.25
0.00	0.00	0.00	-0.75	-0.75
-1.25	-1.25	0.00	-1.25	0.00
-4.50	-4.25	+0.25	-6.00	-1.50
+0.50	+0.50	0.00	+0.25	-0.25
+1.00	+1.00	0.00	+1.25	+0.25
0.00	-0.25	-0.25	-2.75	-2.75
+1.25	+1.25	0.00	-0.50	-0.75
-2.25	-3.00	-0.75	-3.00	-0.75
+1.50	+1.00	-0.50	+0.25	-1.25
+1.50	+1.25	-0.25	0.00	-1.50
-2.75	-3.25	-0.50	-2.50	+0.25
-2.75	-3.25	-0.50	-2.75	0.00
0.00	0.00	0.00	-0.62	-0.62
0.00	0.00	0.00	-0.75	-0.75
+5.00	+5.00	0.00	+6.00	+1.00
+5.00	+5.00	0.00	+5.00	0.00
+4.75	+5.00	+0.25	+5.25	+0.50
+7.50	+7.25	-0.25	+7.25	-0.25
+1.25	+1.75	+0.50	+0.50	-0.75
+1.50	+1.75	+0.25	+1.25	-0.25
-7.00	-7.00	0.00	-7.75	-0.75
-7.00	-7.00	0.00	-6.75	+0.25

\* The data for each pair of eyes are presented as a unit. Errors for the objective methods are computed.

TABLE 6  
SUMMARY OF RESULTS OBTAINED

Noncycloplegia—52 Eyes		Cycloplegia—37 eyes	
Refractometer	Retinoscope	Refractometer	Retinoscope
Average of errors in sphere 0.77 diopters		Average of errors in sphere 0.47 diopters	
Mean of errors in sphere -0.61 diopters		Mean of errors in sphere -0.36 diopters	
Standard deviation of distribution of errors in sphere 0.86		Standard deviation of distribution of errors in sphere 0.47	
Critical ratio of standard deviations 6.1		Critical ratio of standard deviations 1.45	
Failure to find the astigmatic correction 22 instances		Failure to find the astigmatic correction 12 instances	
Finding astigmatic correction when there is none 0 instances		Finding of astigmatic correction when there is none 2 instances	
Errors in cylinder axis of more than 45° 3 instances		Errors in cylinder axis of more than 45° 3 instances	
Average of errors in axis when cylinder is found objectively and subjectively 16.4 degrees		Average of errors in axis when cylinder is found objectively and subjectively 17.8 degrees	
Average of errors in cylinder 0.48 diopters		Average of errors in cylinder 0.36 diopters	
Mean of errors in cylinder +0.23 diopters		Mean of errors in cylinder +0.18 diopters	
Standard deviation of distribution of errors in cylinder 0.59		Standard deviation of distribution of errors in cylinder 0.45	
Critical ratio of standard deviations 3.18		Critical ratio of standard deviations 2.22	

pointed out that, in retinoscopy, a retinal image must serve as the light source for the reflex. Any factors such as spherical aberration, coma, and irregular astigmatism which interfere with the uniformity and sharpness of this illuminated retinal area will cause the reflex to appear less sharp and distinct, aside from the fact that these same factors are manifested as part of the reflex itself.

The larger the pupil, the more exaggerated are these effects, and, conversely, the smaller the pupil, the less important are these factors in producing a disturbance in the reflex.

When cycloplegics and mydriatics are not used, the accuracy of retinoscopy may be enhanced as a result of the increase in sharpness of and the decrease in or elimination of disturbances in the reflex except when the pupil is very small and the direction of the reflex movement is difficult to distinguish.

These concepts are supported by the experimental data which indicate that small-pupil retinoscopy allows for slightly greater accuracy with the possible exception of cylinder-axis determination.

Since the determination of cylinder axis by retinoscopy depends upon placing the axis of the correcting cylinder parallel to the edge of the reflex, a longer reflex edge as a consequence of the increased pupillary diameter should produce greater accuracy. However, any benefit in axis determination obtained with a cycloplegic is more than offset by the higher percentage of eyes in which a cylinder could not be found at all as compared to small pupil retinoscopy.

Any objective means of determining the refractive status of an eye should be accurate and consistent. I have seen no standards or criteria of what constitutes accurate retinoscopy, but in my own experience the great majority of results will be within  $\pm 0.50$  diopters of the subjective findings for both the sphere and cylinder.

From the data of this set of experiments, approximately 89 percent of all eyes ret-

inoscoped without cycloplegics will, for the spherical portion of the correction, be within  $\pm 0.50$  diopters of the subjective finding. With the refractometer, only 36 percent of all eyes examined without cycloplegics will, for the spherical portion of the correction, be within  $\pm 0.50$  diopters of the subjective finding. If an allowance were made for the mean error of  $-0.61$  diopters for the refractometer and only those eyes falling within  $\pm 0.50$  diopters of the mean were included, the number of eyes expected to fall within these limits would be 44 percent.

Applying these same concepts to the cylinders for the noncycloplegic eyes, approximately 80 percent of the retinoscope cylinders could be expected to fall within  $\pm 0.50$  diopters of the subjective value in contrast to 56 percent for the refractometer. With cycloplegia the number of spheres falling within the above limits is decreased to 77 percent for the retinoscope and increased to 58 percent for the refractometer. As for the cylinders under cycloplegia, the relationship for those cylinders found by the two methods remains about the same as for noncycloplegia.

#### CONCLUSIONS

In a series of 89 eyes examined objectively with the Rodenstock Eye-Refractometer and the Reid streak-retinoscope, it has been found that the refractometer is less accurate than the retinoscope in approaching the subjective correction. Cycloplegia increases the accuracy of the refractometer and tends to decrease the accuracy of retinoscopy.

The mean time required for the refractometer for a pair of eyes is about four minutes and is approximately the same as that required for the retinoscope.

The refractometer is less satisfactory than the retinoscope for aphakic eyes and eyes with disturbed medias and pathologic conditions of the retina.\*

\* Since the completion of this paper another paper on the same subject has appeared in the May, 1954, issue of the *A.M.A. Archives of Ophthalmology*.

## NOTES, CASES, INSTRUMENTS

### A CASE OF SYRINGOMYELIA\*

ASSOCIATED WITH VASCULAR ANOMALIES  
OF THE EYES

NORMAN YOURISH, M.D., NATHANIEL  
WOLLIN, M.D., AND ARTHUR  
NATHANIEL, M.D.  
New York

The purpose of this paper is to report a case of syringomyelia and syringobulbia with a number of positive eye findings including several that were unique.

#### CASE REPORT†

*History.* This 60-year-old white woman gave a reliable history.

Her neurologic disease started in 1920 at the age of 35 years when she noted numbness of the left shoulder extending into the left hand. In the next three years she developed weakness of the left arm and difficulty in walking. Her left arm lost pain and temperature sensation at this time. In 1926, (aged 41 years) she noted numbness of the right hand and weakness of the right arm and shoulder. At this time she had intermittent pains in the legs and right arm. She noted that she no longer had temperature sensations in either hand.

From 1928 to 1940, she had increasing weakness of both upper and both lower extremities so that she became bedridden. She was hospitalized as a chronic neurologic case in 1945. At about that time she complained of urinary incontinence and she noticed that, on looking laterally, objects seemed to move or become blurred.

Her family history was noncontributory.

*Neurologic examination.* The patient had bilateral concentric hypesthesia of the face which was present in an onion-peel type dis-

tribution with sparing of the perinasal and perioral regions. There was diminished corneal sensitivity on the left. The pharyngeal reflex was absent on the left. There was analgesia or hypalgesia bilaterally involving the entire body from the face and cervical region down to the toes, except for sparing of the perianal area and one narrow band of relative sensitivity about the waist.

*Eye examination.* Vision was 15/80 in the right eye and 15/40 in the left eye.

On external examination several positive findings were found. Mild ptosis and miosis were present on the left side. The left pupil did not dilate on instillation of four-percent cocaine. Bilateral, rapid clockwise rotary nystagmus was present in all fields of gaze. Corneal hypesthesia was present in the left eye.

The conjunctival and subconjunctival vessels of both eyes showed marked widening and tortuosity of the veins. These seemed to be increased in number and also in diameter. The veins were not accompanied by arteries of equal size but many small arterial twigs were seen around them and many fine arteriolar twigs were noted in the episcleral tissue about the limbus, giving almost the appearance of a ciliary flush (fig. 1).

*Fundus examination* of the right eye showed marked widening and tortuosity of the veins with only slight widening of the arteries. Just nasal to the disc two large dilated loops of veins could be seen apparently arising from the superior nasal vein. A



Fig. 1 (Yourish, Wollin, and Nathaniel). External appearance of eyes, showing dilated vessels beneath the conjunctiva.

\* From the Eye Department, Service of Dr. S. A. Fox, Goldwater Memorial Hospital, Welfare Island.

† Neurologic data were supplied by Dr. N. Finkel.



dilated saccular aneurysm could be seen on the temporal side of the disc, arising from the superior temporal artery. The eyegrounds of the left eye were normal.

#### COMMENT

Our case shows a number of typical eye manifestations, one or more of which can be present in this disease. Rotary nystagmus is commonly present. The site of the disturbance is not certain. It has been variously suggested that it is due to involvement of the spinocerebellar pathways,<sup>1</sup> to disturbance of the vestibular nuclei or their central connections,<sup>2</sup> or to disturbances of the descending vestibular nerve.<sup>3</sup>

Horner's syndrome is a characteristic finding, although ptosis and miosis may be minimal. Since syringomyelia usually starts in the cervical cord, Horner's syndrome is seen early, due to involvement of the ciliospinal center or its pathways.<sup>2, 4</sup>

Loss or diminution of corneal sensitivity has been described and is due to destruction of the descending tracts of the trigeminal nerve.<sup>2, 5</sup> Other findings, which were not present in this case, but can occur in this disease, are optic atrophy, papilledema, muscle palsy, and lagophthalmos.<sup>1, 2, 4, 5</sup>

The unusual eye findings in our case were the presence of abnormal conjunctival and episcleral blood vessels, as well as the marked dilatation and tortuosity of the retinal veins in the right eye. We do not believe this clinical picture has previously been reported in conjunction with syringomyelia. The pres-

ence of the anomalous vascular pattern in the eyes suggested the possibility that similar vascular malformations might be present in the cervical and bulbar regions.

Examination of recent neurologic literature revealed that there has been increasing recognition of vascular neoplasms and malformations as a common cause of syringomyelia.<sup>3, 6, 7</sup> Although cavitations of the spinal cord can occur in a variety of conditions Netsky concludes a recent clinicopathologic study by stating that "it is suggested that an intramedullary vascular anomaly of the spinal cord is the cause of 'true' syringomyelia."<sup>6</sup> However, in none of these reports were any vascular anomalies noted in the eyes.

Wyburn-Mason described a group of cases with arteriovenous aneurysms of the mid-brain and retina, associated with facial nevi in some instances.<sup>8</sup> These cases all had unilateral retinal involvement and symptoms of mid-brain disease. In his monograph, Wyburn-Mason links syringomyelia closely to Lindau's disease.<sup>9</sup> He feels that the lesion in the cord is an intramedullary hemangioblastoma which may be silent or may be manifested as syringomyelia. Some of the cases in his series had visceral and retinal involvements as well.

This evidence is very suggestive that our patient has a congenital vascular anomaly of the eyes, brain stem, and cord which does not fit readily into any of the syndromes mentioned.

*Goldwater Memorial Hospital.*

#### REFERENCES

1. Duke-Elder, W. S.: *Textbook of Ophthalmology*. St. Louis, Mosby, 1949, v. 4, p. 4231.
2. Walsh, F. B.: *Clinical Neuro-ophthalmology*. Baltimore, Williams & Wilkins, 1947, pp. 743-745.
3. Taylor, J., Greenfield, J. G., and Martin, J. P.: Two cases of syringomyelia and syringobulbia observed clinically over many years and examined pathologically. *Brain*, **45**:323-356, 1922.
4. Tassman, I. S.: *The Eye Manifestations of Internal Diseases*. St. Louis, Mosby, 1946, ed. 2, pp. 543-544.
5. Kestenbaum, A.: *Clinical Methods of Neuro-ophthalmological Examination*. New York, Grune and Stratton, 1946.
6. Netsky, M. G.: Syringomyelia, *AMA Arch. Neur. & Psychiat.*, **70**:741-777, 1953.
7. Brion, S., Netsky, M. G., and Zimmerman, H. M.: Vascular malformations of the spinal cord, *AMA Arch. Neur. & Psychiat.*, **68**:339-361, 1952.
8. Wyburn-Mason, R.: Arteriovenous aneurysms of midbrain and retina. *Brain*, **66**:163, 1943.

9. Wyburn-Mason, R.: *The Vascular Abnormalities and Tumors of the Spinal Cord and Its Membranes*. London, Kimpton, 1943, p. 60.

## STREPTOKINASE AND STREPTODORNASE\*

IN INTRAOCULAR HEMORRHAGE

ARTHUR SACKS-WILNER, M.D.  
*Trenton, New Jersey*

AND

S. SINCLAIR, M.D., AND  
TRUMAN BOYES, M.D.  
*New York*

Tillet and Sherry showed that blood clots and the related coagulum of exudates are rapidly lysed when concentrated and partially purified preparations derived from broth cultures of hemolytic streptococci are instilled into them. Hence, preparations show rapid lysis of fibrin and cause the insoluble fibrouslike nucleoprotein found in purulent collections to dissolve.

The fibrinolytic activity of hemolytic streptococci was discovered by Tillet and Garner. Sherry, Tillet, and Christensen showed that a significant constituent present in pus consisted of desoxyribonucleoprotein, forming 30 percent to 70 percent of purulent sediment. A second enzyme, desoxyribonuclease, changed the thick nucleoprotein to a thin solution. The streptococcal fibrinolysin product has been termed "streptokinase," and the nucleoprotein lysing factor, "streptodornase" (desoxyribonuclease). In summary, (a) streptofibrinolysin (streptokinase) is the fibrinolytic principle derived from hemolytic streptococcus; (b) streptodornase is the principle acting on nucleoprotein (streptodesoxyribonuclease) or the pus-liquefying enzyme. In general, the concentrates contain 6,000 units of nuclease to 15,000 units of streptokinase.

The normal clotting mechanism is well known. By the action of thromboplastin (or

thrombokinase), prothrombin, which is inactive, is converted in the presence of calcium ions into the active thrombin. Thrombin, an enzyme, then acts upon the soluble fibrinogen of the plasma to convert it into the insoluble fibrin, which has been described as forming threads in which the solid elements of the blood are enmeshed. Thus, the clot is formed. When bleeding occurs, the thromboplastin is liberated from the injured tissues by fragmentation of platelets; thus the clotting mechanism is initiated.

Jukofsky used the streptokinase-streptodornase combination experimentally in the treatment of artificially produced hyphema in the anterior chamber of rabbits. He found that concentrations of 50,000 units of the streptokinase-streptodornase combination aided in lysing clotted blood; at this concentration, some of the unfavorable reactions, obtained when higher concentrations were used, could be avoided. He also stated that, when the concentrations were below 50,000 units, the reaction was lessened but the effectiveness in the fibrinlysing process remained.

In view of these reports, it seemed feasible, theoretically at least, to use this substance in cases of intraocular hemorrhage. The following reports of two cases of intraocular hemorrhage describe our findings.

### CASE REPORTS

#### CASE 1

R. C., a 79-year-old white man, had vision of hand movements at one foot, O.U., with good light perception and projection. The vision had supposedly been the same for the past two years. Diagnosis was vitreous hemorrhage, bilateral, etiology unknown. On June 23, 1953, 100 units of streptokinase-streptodornase were injected into the vitreous, 12 mm. behind the limbus in the upper outer quadrant, with a 27-gauge needle, which was sparked with diathermy as it was removed from the globe. The iris was well

\* From the Department of Research, New York Eye and Ear Infirmary.

dilated with atropine prior to injection.

The next day, the tension was 23 mm. Hg. (Schiotz) and there were tension marked chemosis of bulbar conjunctiva and ciliary injection. The pupil was moderately dilated. There was a two-plus flare but the retinal reflex was somewhat better. The vitreous appeared clearer.

Cortone solution (2.5 percent) was started every two hours and atropine (one percent), three times a day.

Three days later, the retinal vessels could be seen as the vitreous had become progressively clearer. Vision in the right eye was counting fingers at one foot, with good light perception and projection. Several large isolated hemorrhages could be seen in the vitreous. It was suggested that further small injections should be given but the patient refused. He was last seen December 30, 1953, at which time he was able to count fingers and the retina was easily visible. Further therapy was again suggested but refused.

## CASE 2

D. O., a 57-year-old white woman, a known diabetic, had faulty light projection in both eyes, better in the right eye than in the left. Vision has been about the same for the past three years.

Retinal detachment and vitreous hemorrhages were present, O.U. No fundus reflex was seen in either eye. On May 26, 1953, 200 units of streptokinase-streptodornase were injected into the vitreous of the right eye, using the same technique as in Case 1. The next day, tension in the right eye was 38 mm. Hg. There was a marked reaction, with chemosis of bulbar conjunctiva, edema of lids, a four-plus flare, and cells in the anterior chamber, posterior synechias, and iris pigment migration. Every attempt was made to dilate the pupil with little success.

The tension gradually dropped to normal on atropine and cortisone solution locally every two hours.

A white fibrinous exudate developed in

the anterior chamber one week after the injection, and completely disappeared in three days. The eye continued to be irritated, with ciliary injection and a three-plus flare for the next month and a half. Tension remained normal. During this time no fundus reflex was visible.

On July 21, 1953, streptokinase-streptodornase (500 units) was injected into the vitreous of the same eye by the identical technique. The next day a fine, grayish membrane developed over the pupillary area. Lid edema and ciliary and conjunctival injection were present. The anterior chamber was shallow with the tension, right eye, 60 mm. Hg. and a four-plus flare and cells in the anterior chamber. The cornea was edematous.

During this time, the patient was continually on atropine and 2.5-percent cortone. The tension gradually dropped to normal in two weeks. There were extensive anterior peripheral synechias; corneal edema persisted; the anterior chamber was shallow; there was a four-plus flare. No fundus reflex could be seen at any time. The eye became phthisical after about four months. The vitreous did not clear after either procedure. The patient was in severe pain during most of this time; however the pain gradually subsided. The result was poor.

## DISCUSSION

Friedman treated two cases of subconjunctival hemorrhage with streptokinase-streptodornase with poor results and three patients with hyphema with equally poor results. In all patients, there were severe reactions. Dosages ranged from 35,000 units to 50,000 units. In one case, the secondary glaucoma and pain were so severe as to require enucleation.

Roberts and Barton reported, as they stated, their two unfortunate cases of hyphema. In one case, injections of streptokinase-streptodornase were made into the anterior chamber; subconjunctivally in the other. Both had severe iridocyclitic responses and secondary glaucoma, and the results, as stated, were very poor.

Of our two cases, one had an exceedingly poor result; the other showed improvement after injections of small amounts. The severe reactions and other findings were almost identical to those of Friedman and Roberts and Barton.

It becomes increasingly clear that to inject streptokinase-streptodornase intraocularly is fraught with danger and should not be attempted in usually self-limiting condi-

tions. In otherwise hopeless cases, and for want of anything better at this time, small doses, not higher than 100 units, may be injected intravitreally, if the iris is kept well dilated and cortisone therapy is started immediately.

Further studies should be attempted to evaluate the effectiveness of this substance in intravitreal hemorrhage.

225 West State Street.

#### REFERENCES

- Friedman, M. W.: Streptokinase in ophthalmology. *Am. J. Ophth.*, **35**:1184 (Aug.) 1952.  
 Jukofsky, S. L.: A new technique in the treatment of hyphema. *Am. J. Ophth.*, **34**:1692 (Dec.) 1951.  
 Read, C. T., and Berry, F. B.: The utilization of streptokinase-streptodornase in a patient with hemo-pneumothorax and a patient with postpneumectomy sanguinous coagulum. *J. Thoracic Surg.*, **20**:382, 1950.  
 Sherry, S., Tillet, W. S., and Christensen, L. R.: The use of streptokinase-streptodornase in the treatment of hemothorax. *J. Thoracic Surg.*, **20**:393, 1950.  
 Tillet, W. S., Sherry, S., and Christensen, L. R.: *Proc. Exper. Biol. & Med.*, 1948.  
 Tillet, W. S., and Garner, R. L.: Fibrinolytic activity of hemolytic streptococcus. *J. Exper. Med.*, **58**:485 (Oct.) 1933.

### CONGENITAL NEUROPARALYTIC KERATITIS\*

WALTER SEGALL, M.D.  
Chicago, Illinois

Because there is usually a systemic cause, ulceration of the cornea in infants presents an interesting problem. In the two cases here presented, the corneal ulceration was associated with congenital malformations and it was difficult to determine whether keratomalacia or a congenital defect of the first division of the trigeminal nerve caused the condition. Only two similar cases could be found in the literature. These will be discussed later.

#### CASE REPORTS

##### CASE 1

R. L., aged six months, a white boy, was admitted to the Children's Memorial Hospital because his mother noticed a grayish discoloration in both eyes. This was his second

admission, the first being shortly after birth when a cleft lip was repaired.

*Past history.* Spontaneous delivery had followed an eight-month pregnancy. Birth weight was seven lb., five oz. The child had a cleft lip and a cleft palate which involved the hard and soft palates and the uvula. Present also were deformities of the right auricle and the right ear canal, a cervical spina bifida, and anomalies of both thumbs. The X-ray report suggested the Klippel-Feil syndrome.

*Eye examination.* Both eyes presented similar pictures. The conjunctivas were normal; the eyeballs only slightly congested. In the center and below each cornea were large ulcers, about four mm. in diameter, which had a dry appearance.

The pupils were small; the fundi could not be seen.

*Diagnosis.* The tentative diagnosis of keratomalacia was based on the dry-appearing ulcers and on the general state of malnutrition.

*Treatment.* Penicillin was given systemically and several antibiotics were used locally.

\* Presented before the Chicago Ophthalmological Society, January 18, 1954.



In addition, oleum percomorphum, 0.5-percent cortisone, one-percent atropine, and 10-percent neosynephrine were administered. Both eyes were covered for long periods. Zyma drops were given orally and, later, vitamin A in aqueous solution was administered intramuscularly.

The antibiotics were changed frequently because none of them was effective. Local cortisone seemed to make the ulcers worse. The best results followed covering the eyes.

In accordance with the diagnosis of keratomalacia, a vitamin-A absorption test was made. It showed a flat (absorption) curve. This did not change even after daily high doses of vitamin A over a long period. In that respect this case differed from a true keratomalacia, which is believed to be due to an insufficient supply of vitamin A. In rare cases, keratomalacia may be caused by insufficient absorption of vitamin A due to such disturbances as celiac disease or fibrocystic conditions of the pancreas. Such conditions could be excluded in this patient,

since the stools and the trypsin test were normal.

*Eyes.* The pupils were small and did not dilate under atropine or neosynephrine (10 percent). The child kept both eyes wide open and did not show any sign of pain, although deep corneal ulcers were present. There were no tears and the blink reflex was rarely visible. The corneal reflex to touch revealed complete anesthesia of both eyes and to some extent of the surrounding skin. The consultant in neurology, Dr. Buchanan, confirmed these findings and reported:

"Anesthesia of right cornea, severe hypalgesia of left cornea, bilateral facial weakness, anomaly of right ear, anomaly of right side of tongue, cleft palate, cervical spina bifida with probably a Klippel-Feil syndrome, congenital defect of the ribs. The most remarkable is the corneal anesthesia, right and left, presumably congenital. The corneal ulceration is related to this anesthesia."

When the corneal ulcer threatened to perforate, tarsorrhaphy was contemplated. For-

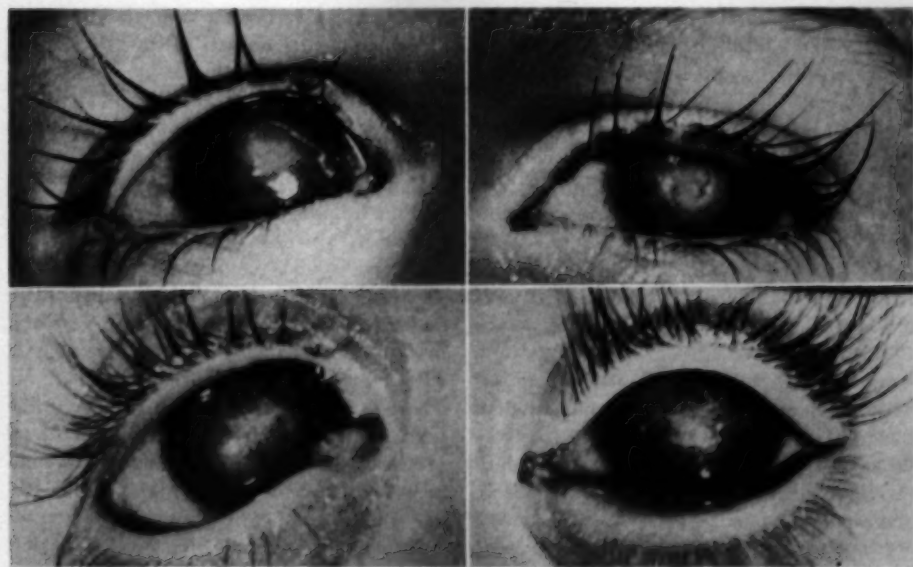


Fig. 1 (Segall). *Case 1.* (Above) Appearance of eyes on February 26, 1953. (Below) Appearance of eyes on May 20, 1953.



unately the condition improved and surgery was not necessary. The eyes did not show any congestion, nor were there any signs of pain even when the disease had reached the culmination point.

The ulcers improved very slowly, blood vessels began growing toward the center of the ulcer. At this stage, the child was discharged from the hospital.

At home he received ample vitamin therapy, locally atropine, aureomycin ointment, and prolonged covering of both eyes. Further observation in the out-patient department showed that the child gained weight and the thick corneal infiltrates became absorbed; however, a small, angular, central scar formed and optical nystagmus developed.

#### CASE 2

B. K., a boy, was delivered by forceps. Birthweight was seven lb., nine oz. The mother had a hemorrhage at one and one-half months of pregnancy, successfully treated with bedrest.

In the first few weeks the child had nutritional difficulties together with a skin rash. These disappeared with changes in the diet. He received an ample vitamin supply.

At about his fifth month, the mother noticed a grayish discoloration in the left eye. The pediatrician referred the child to me and he was admitted to Children's Memorial Hospital with the diagnosis of keratomalacia.

*On pediatric examination* (Dr. John A. Bigler) the baby was irritable. He had several scratches on the face. The head, which could not be held up, was asymmetric and turned to the right side (right torticollis). The left mandible was less prominent than the right, and the left side of the face was flattened and receded, in comparison with the right side. There was an inguinal hernia and signs of malnutrition.

*Eye examination.* The eye findings were similar in both eyes, differing only in degree. The corneal reflex to touch and the blink reflex were absent. There were no tears on

crying. Ointment applied to the eyeball stayed on the same spot till it melted. The child poked his eyes with his fingers, especially after awakening in the morning, so that his arms had to be restrained.

The conjunctivas in both eyes were normal in appearance. The right eye was white and showed only a small epithelial defect in the center of the cornea; the left eye was somewhat congested and had a superficial, large (about three mm.) ulcer in the center of the cornea.

The edges of the ulcer were infiltrated and the surrounding cornea was slightly opaque. Both pupils were small and did not dilate under atropine or 10-percent neosynephrine. The left iris had a reddish sheen which disappeared gradually with improvement of the ulcer. A good red reflex was visible in the right eye, none in the left. Fundus details could not be made out.

The vitamin-A absorption curve was flat. Treatment was similar to that in Case 1. High doses of aqueous vitamin A were given systemically at regular intervals; later the absorption curve became normal. The bowel movements were normal in consistency and the trypsin test gave normal figures.

*The neurologic examination* (Dr. Buchanan) showed no reaction to touch or to painful stimuli in the distribution of the first division of the trigeminal nerve on the right and the left side.

*The X-ray report* (Dr. H. White) was: "There is a congenital anomaly of the ribs on both sides. On the right, the fourth, fifth, and sixth ribs are fused at their vertebral margins. On the left, the fourth and fifth ribs are fused at their vertebral margins. There is also a congenital anomaly of the fifth and sixth, and probably seventh dorsal vertebrae, consisting of incomplete development and incomplete segmentation. The lumbar spine is essentially normal."

*Course.* In the following weeks the left eye improved, leaving only a fine diffuse opacity; however, the right eye developed an irregular, superficial ulcer (about four

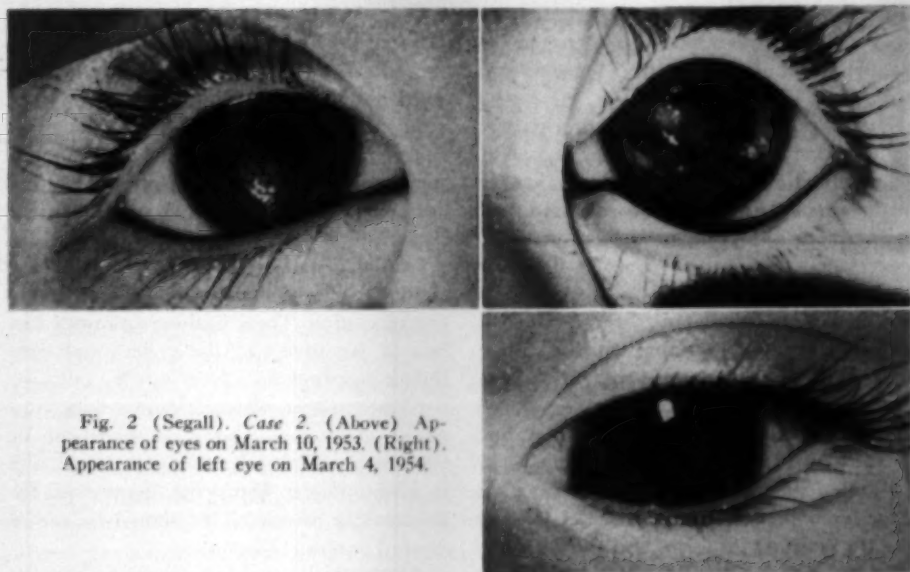


Fig. 2 (Segall). Case 2. (Above) Appearance of eyes on March 10, 1953. (Right). Appearance of left eye on March 4, 1954.

mm.) which slowly improved under antibiotic ointments and covering.

About four months after onset, the ulcers in both eyes cleared up leaving only a fine, diffuse, central opacity in both eyes, worse in the right, giving them a slight milky appearance.

The pupils dilated very little under atropine or neosynephrine. Antibiotic ointments seemed to have little effect on the outcome. Covering both eyes appeared to be more beneficial than the rest of the treatment.

Several months later a flare-up in one eye was caused by soapy water. Covering the eye, atropine, and sulfadiazine ointment improved the condition within a short time. At present the child gets sulfadiazine ointment in both eyes once daily.

#### COMMENT

These were the predominant symptoms in the two reported cases:

1. Ulceration of the cornea with loss of corneal sensitivity and corneal reflex in both eyes. The conjunctivas were normal in appearance.

2. Apparently a disturbance in the autonomic nervous system was manifested by the absence of any vasomotor reaction and by the miotic pupils which barely reacted to atropine or neosynephrine.

3. A spina bifida (in R. L. in the cervical spine, in K. B. in the dorsal spine). Both children had abnormalities of the ribs.

4. Malnutrition and disturbance in the absorption of vitamin A.

5. The disease began about the fifth month and ended, several months later, with formation of the relatively thin scar.

#### DISCUSSION

The eye and the surrounding area are supplied by the first branch of the trigeminal nerve which transmits not only the normal sensations of the cornea, conjunctiva, and eyeball, but also supplies the afferent part of several reflexes important in the protection of the eye. If there is a lesion somewhere in the trigeminal nerve, in the Gasserian ganglion, or in the supraganglionic tracts, with disturbance in the sensation of the cornea and consequent elimination of the

afferent part of the reflexes, a keratitis may develop because of corneal exposure to the outside air without a normal defense mechanism.

Exposure seems to be an integral part in the development of keratomalacia as well as neuroparalytic keratitis. The ulcer is located in the exposed part of the cornea and does not react to any form of medical therapy. Covering is the most effective treatment. It heals with the formation of a scar which is more resistant to external damage.

These conditions were present in my cases as was the interesting fact that the lesion was congenital. The keratitis may have developed at about the fifth month because, at that period of life, the sleeping time gets shorter and the number of hours with the eyes open increase. The reflex to touch was missing and no sense of pain could be elicited.

In addition to the trigeminal abnormality, a defect in the autonomic nervous system seemed to be present. This was manifested by the absence of any vasomotor reaction of the globe despite the severity of the lesion, and in the miosis of the pupils which did not react to atropine or 10-percent neosynephrine. It is easy to understand that the pupils did not dilate during the keratitis even under strong mydriatics since some iritis and spasm of the iris are always combined with it. In my cases the miosis persisted even after the inflammation had subsided, although no synechias were present. The persistent miosis and the lack of congestion suggest a defect in the autonomic nervous system.

Finally, the abnormal vitamin-A absorption should be mentioned. It was permanent in R. L.; however, B. K. showed improvement under high oral and parenteral doses of aqueous vitamin A. It is not possible to say what connection there is between vitamin-A deficiency and anesthesia of the first division of the trigeminal nerve. Yet this is important to a real understanding of the cause of the corneal disease.

Duke-Elder mentions two other eye diseases in the differential diagnosis for neuroparalytic keratitis—keratitis e lagophthalmo and keratomalacia. The etiology of keratitis e lagophthalmo is obvious and will be excluded from this discussion. The other two, keratomalacia and neuroparalytic keratitis have much in common and show great variation in degree.

One may find dryness of the cornea and conjunctiva, exfoliation of the epithelium, and ulceration. There is always more or less loss of sensitivity of the eyeball and very little congestion.

Keratomalacia, which is caused by a vitamin-A deficiency, shows improvement or even recovery in early cases if a proper diet is given, unless fibrocystic disease of the pancreas is present. This should be useful for a differential diagnosis.

Although my patients were undernourished, they did not develop the keratitis at the lowest ebb of their nutritional status but much later at the fifth month of life at a time after they had received an adequate diet with ample supplies of vitamins and when their weights were increasing. Furthermore, the eye condition did not improve, in fact the ulcers in the first child became worse while high vitamin-A doses in aqueous solution were given. These findings do not seem to be in agreement with the diagnosis of keratomalacia.

In both conditions there is a disturbance in the sensitivity—in keratomalacia due to a degeneration of the nerve endings; in neuroparalytic keratitis due to a lesion somewhere in the course of the trigeminal nerve. In the first disease the disturbance in sensitivity is limited to the eye itself; in neuroparalytic keratitis, it also affects the surrounding skin.

Mellanby produced xerophthalmia in animals experimentally by diets deficient in vitamin-A and carotene. He states:

"It (xerophthalmia) may be secondary to a loss of neurotrophic control normally exerted on the cornea by the ophthalmic divi-

sion of the trigeminal nerve."

Although the keratitis may be of severe degree, there is very little congestion in either keratomalacia or neuroparalytic keratitis.

Duke-Elder mentions keratomalacia in persons with adequate diet and apparently in good health who show no response to the usual treatment and he suspects an etiology of excessive growth with abnormal high vitamin consumption. Considering the observations in my two cases, one wonders if a neurotrophic defect in the trigeminal nerve could be present in the patients Duke-Elder describes.

Two cases of "congenital neuroparalytic keratitis" are described in the literature. In Kayser's case, both grandfathers of the child had neurosyphilis. Birth weight was normal. There was a feeding problem due to difficulties in sucking and swallowing. On the ninth day the first eye symptoms, small, round, epithelial defects in the exposed parts of both corneas, appeared. There was no irritation in either eye. Exacerbation of these ulcerations occurred frequently up to the child's death of pneumonia at the age of three and one-half years. Kayser suspected a centrally located trigeminal defect.

There is a great similarity between Kayser's patient and my reported cases. In both instances the children were born after normal pregnancies, with normal birth weights, but with feeding problems. The epithelial defects and the ulcers developed in both eyes at an early age. There was no corneal or conjunctival congestion but both organs were completely insensitive. The sensitivity of surrounding skin was also reduced. The ulcer developed only in that part of the cornea which was exposed to the air and healed with a scar. The physical development of the children was retarded.

Lawford reported the second case. He describes a large, shallow, irregular ulcer of the left cornea in a six-year-old child without

hypopyon and with very little congestion. The ulcer healed in three weeks under patch and mydriatics. There was a bilateral anesthesia of the conjunctiva and cornea, although only the left cornea ulcerated. There was no loss of sensation in the skin or in the mucosal membrane supplied by the trigeminal nerve.

Several differences between Lawford's patient and my cases are apparent, the most important being the time of onset, the duration of the disease, and the area affected by the anesthesia. In both my cases, the eye disease was bilateral, developed early in life, and took several months to heal. The anesthesia was not restricted to the eyeball but extended to the surrounding skin. These differences make one doubt Lawler's classification of his case as one of "congenital neuroparalytic keratitis," which doubt the author also expressed by adding a question mark before the word congenital.

#### SUMMARY

A symptom complex, observed in two infants, is characterized by a keratitis beginning with a central corneal epithelial defect which may develop into extensive ulceration. The eyes in the reported cases were not congested. Covering was the most effective treatment. The children were undernourished and there was a disturbance in vitamin-A metabolism. The X-ray films showed developmental anomalies of the spine and ribs in both children.

A congenital disorder in the area supplied by the first branch of the trigeminal nerve seems to be the cause of the corneal ulcers, hence the designation of "congenital neuroparalytic keratitis." This title does not, however, suggest the two other important characteristics of the disease—the changes in the skeleton (spine and ribs) and the disturbance in the vitamin-A metabolism.

11106 South Michigan Avenue (28).



## REFERENCES

- Duke-Elder, W. S.: *Textbook of Ophthalmology*. St. Louis, Mosby, 1940, v. 2, p. 1958.
- Kayser, B.: Ein Fall von angeborener Trigeminauslaehmung und angeborenem Traenenmangel. *Klin. Monatsbl. f. Augenh.*, **66**:652, 1921.
- Lawford, J. B.: Bilateral (congenital?) anaesthesia of conjunctiva and cornea, neuroparalytic keratitis. *Tr. Ophth., Soc. U. Kingdom*, **17**:80, 1907.
- Mellanby, E.: Xerophthalmia, trigeminal degeneration and vitamin-A deficiency. *J. Path. & Bact.*, **38**:391, 1934.
- Sommer, I., and Spiegel, E. A.: *Neurology of the Eye, Ear, Nose, and Throat*. New York, Grune, 1944, p. 467.

### ALTITUDINAL HEMIANOPSIA AND PAPILLEDEMA\*

B. G. PRATER, M.D., AND  
ROBERT L. LAM, M.D.  
*Saint Louis, Missouri*

Altitudinal field defects are rare. As far as could be ascertained there has been no reported occurrence of this phenomenon with papilledema. It was thus felt that the following case study would be of interest.

#### CASE REPORT

P. S. (225066), a 17-year-old white youth was admitted July 10, 1953, to the Neurology Division of the Barnes Hospital with the chief complaint of ocular pain, visual disturbances, fever and malaise. A dull generalized headache with the malaise had been noted three weeks before admission.

Fever about 104°F. was treated by small doses of penicillin and chloramphenicol administered by his family doctor. This resulted in symptomatic relief. However, two weeks before admission, the patient suffered an acute onset of loss of vision in the inferior field of the right eye.

This began with two small blind spots, which enlarged within two or three hours to include, sharply, the entire lower one half of the visual field in the right eye with striking sparing of the upper half. Ocular pain was not again experienced until one week later when he noted a dull pain in both eyes.

In spite of his visual disturbance and mild generalized weakness, he returned to his

job on the assembly line of an auto-body company. The hemianopsia during this period was described as "black with tiny moving white dots, like germs."

On the night before admission he felt unsteady, tired, somewhat confused, and dulled in sensorium; the pain in the right eye increased in intensity and was associated with a bifrontal and bitemporal headache. He had cramping pains in both lower extremities and the right shoulder and upper extremity. The past history was essentially noncontributory.

*Physical examination* showed temperature: 39.2°C., pulse: 80, respirations: 20, and blood pressure: 128/60. The patient complained of cramps in the thighs on movement of the lower extremities. The remainder of the medical examination was within normal limits.

*Neurologic examination* revealed no abnormality in gait or station except the presence of cramping pain in the thighs while walking. No localized weakness, although a mild degree of generalized decreased muscle strength was noted. All deep tendon reflexes were active and equal bilaterally. No pathologic reflexes were elicited. Superficial skin reflexes were present.

No sensory abnormalities were found except in vision. No evidence of cerebellar dysfunction could be demonstrated. Cranial nerves were normal except for the optic. Mental status was not unusual. No meningeal irritation signs were found.

*Ophthalmologic examination* demonstrated acuity of 6/6, O.D.; 6/6, O.S. The ocular adnexa, conjunctiva, and sclera were normal. Testing of extraocular muscles revealed

\*From the Departments of Ophthalmology and Neuropsychiatry and The Oscar Johnson Institute, Washington University School of Medicine.



normal ductions and versions. The pupils were round, regular, equal, and reacted well to light and accommodation and consensually. Corneal reflexes were present.

Intraocular pressure was normal and there was no tenderness of the globes. Findings on slitlamp examination were within normal limits.

*Ophthalmoscopic examination* revealed the media to be clear. There was a definite two-diopter elevation of both nerveheads with a complete loss of physiologic cupping and blurring of the disc margins. The juxtapapillary areas were grayish in appearance. All arteries and arterioles appeared normal, and the bifurcations of the central retinal arteries were clearly visible. Mild but definite dilatation of the veins was present. No hemorrhages or exudates could be found. The maculas were not unusual and showed normal foveal reflexes. The periphery of the retinas

demonstrated no abnormalities.

*Examination of the visual field* disclosed bilateral enlargement of the blindspots and a sharply delimited inferior altitudinal hemianopsia of the right eye with a general sloping constriction of the right superior field (fig. 1).

*Laboratory data.* Complete blood counts, urinalysis, cardiolipin, plasma proteins, and albumin-globulin ratio, complete agglutination studies, complement-fixation tests, and repeated blood cultures were negative. X-ray studies of the skull, chest, and teeth were normal. Electroencephalographic studies showed a slow dysrhythmia with a left central focal trend. The initial lumbar puncture revealed a pressure of 235 mm. of spinal fluid. No pleocytosis, normal proteins, chlorides, sugars, and negative cultures were the results of studies on each lumbar puncture. Subsequent taps indicated normal pressures.

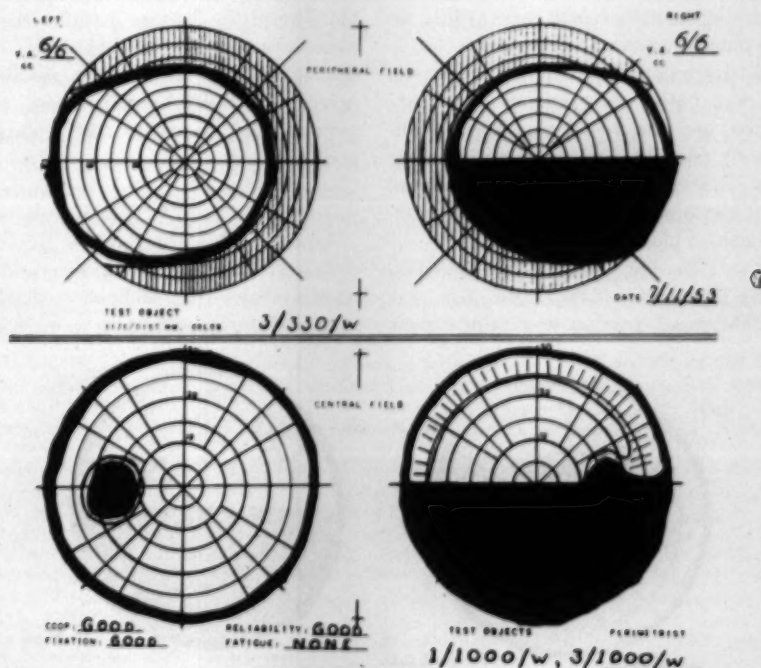


Fig. 1 (Prater and Lam). The right altitudinal hemianopsia is clearly shown on peripheral and central fields. The enlargement of the blindspots is seen on the central fields.

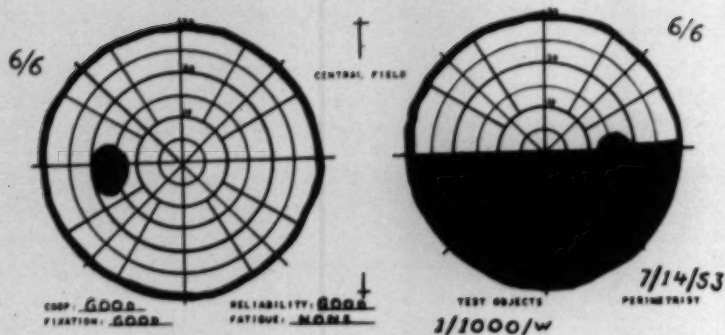


Fig. 2 (Prater and Lam). There is no change in the altitudinal hemianopsia, but the blindspots are shrinking.

*Hospital course.* There was transient nuchal rigidity during the first week of hospitalization without definite spinal fluid changes. In the second week a palpable spleen was found and a questionable diastolic murmur was heard. The patient was given the usual course of penicillin and streptomycin for subacute bacterial endocarditis, although the diagnosis was uncertain.

By the sixth day a decrease in the disc elevation was noted on ophthalmoscopic examination, and the visual field showed improvement (fig. 2). On the 10th day there was no elevation of the right nervehead and minimal elevation of the left. The disc margins remained blurred.

On the 13th day, pallor in the superior temporal quadrant of the right disc was noted. The nasal portion was faintly pale.

The vessels, periphery, and maculas were normal. Visual field tests showed that the blindspots had returned to normal size, and that the absolute altitudinal defect was unchanged (fig. 3).

On discharge, re-examination of the patient revealed only the bilateral residual blurring of the flat disc margins, the marked superior temporal and slight nasal pallor of the right disc, and the sharp, absolute, right inferior altitudinal hemianopsia. On subsequent clinic visits no other changes have been noted.

#### DISCUSSION

Embolism of a branch of the retinal artery, retinal arteritis, arterial spasm, and arterial occlusion are often difficult to differentiate as the etiologic mechanism in unilateral alti-

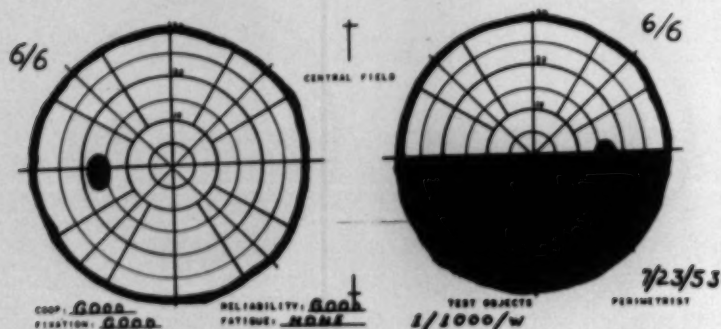


Fig. 3 (Prater and Lam). The blindspots are normal size, but the altitudinal hemianopsia persists.

tudinal defects.<sup>1-3</sup> Hemianopsia of the altitudinal type has been reported with gastrointestinal hemorrhage,<sup>4</sup> in chiasmal defects and multiple sclerosis,<sup>5</sup> following streptomycin therapy in which toxic spasm seemed causative (case examined by one of us, R. L. L.),<sup>6</sup> and following a bullet wound of the optic nerve.<sup>7</sup>

In an altitudinal hemianopsia such as this, the lesion must be located anterior to the chiasm. In the absence of trauma and considering the blood supply to the optic nerve,<sup>8</sup> the clear-cut demarcation shown in this field would be difficult to explain on the basis of a primary nerve defect.

A vascular lesion in the superior retinal artery is most plausible. No evidence of embolism, spasm, thrombosis, or arteritis could be found on admission. However, the initial stages of ischemia of the retina are essentially edematous and are reversible, but on regressing may have dead ganglion cells. The first known field loss occurred about two weeks before admission. Pallor of the nervehead corresponding to the field loss is conclusive evidence of nerve-fiber degeneration.

Optic neuritis is not uncommon in generalized infectious diseases and has been reported in many.<sup>9</sup> Bilateral optic nervehead swelling without field defects and with cen-

tral retinal artery occlusion has been seen with proven subacute bacterial endocarditis.<sup>10-12</sup> Inflammation and demyelination of the nerve usually cause central scotomas and occasionally nerve-fiber defects which lead to loss of visual acuity of a variable and fluctuating nature.

This patient had a febrile disease associated with transient papilledema and a field defect. The papilledema was bilateral and probably not associated with the immediate cause of the field defect. A systemic infectious illness could account for the papilledema on the basis of a serous meningitis. A transient closure of the superior retinal artery on an embolic or spastic basis can explain the altitudinal field defect. Subacute bacterial endocarditis is the most likely diagnosis, and its reported manifestations have been suggestively similar to this case.

#### SUMMARY

A case of altitudinal hemianopsia with corresponding pallor of the optic nervehead and transient bilateral papilledema has been presented. A diagnosis of subacute bacterial endocarditis was suspected but not confirmed by blood culture.

640 South Kingshighway (10).

#### REFERENCES

1. Duke-Elder, W. S.: *Textbook of Ophthalmology*. St. Louis, Mosby, 1945, v. 3, pp. 2561-2578.
2. Mastier, P., and Farnarier, G.: Artérite rétinienne ayant réalisé une hémianopsie horizontale bilatérale et symétrique. *Bull. Soc. d'Ophtal. Paris*, **51**:197, 1939.
3. Grimsdale, H.: A spasm of a branch of the central retinal artery. *Brit. J. Ophthalm.*, **24**:208, 1940.
4. Grout, G. H.: A case of permanent impairment of vision following gastro-intestinal hemorrhage. *Arch. Ophthalm.*, **43**:234, 1914.
5. Brown, H. W.: Altitudinal hemianopsia with bilateral absence of the radial pulse. *Arch. Ophthalm.*, **22**:145, 1939.
6. Schultz, A. E.: Altitudinal hemianopsia during streptomycin therapy. *Am. J. Ophthalm.*, **32**:211, 1949.
7. Traquair, H. M.: *An Introduction to Clinical Perimetry*. St. Louis, Mosby, 1942, ed. 4, p. 200.
8. Wolff, E.: *The Anatomy of the Eye and Orbit*. Philadelphia, Blakiston, 1951, ed. 3, pp. 265, 330-331.
9. Duke-Elder, W. S.: *Textbook of Ophthalmology*. St. Louis, Mosby, 1945, v. 3, p. 3004.
10. Falcone, A. W.: The importance of optic neuritis and retinal hemorrhages in the diagnosis of chronic septic endocarditis. *Quart. J. Med.*, **3**:107, 1909.
11. Dienst, E. C., and Gartner, S.: Pathological changes in the eye associated with subacute bacterial endocarditis. *Arch. Ophthalm.*, **31**:198, 1944.
12. Friedenwald, H. S., and Rones, B.: Some ocular lesions in septicemia. *Tr. Am. Ophthalm. Soc.*, **28**:286, 1930.
13. Dellmann, F. L.: Metastatische Prozesse am Auge bei der Endocarditis lenta. *Klin. Monatsbl. f. Augenheilk.*, **63**:666, 1919.

# SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

## CHICAGO OPHTHALMOLOGICAL SOCIETY

January 18, 1954

DR. GAIL R. SOPER, *President*

The clinical meeting was presented by the Departments of Ophthalmology of the University of Chicago and of Provident Hospital, Dr. Frank Newell, presiding.

### VASCULARIZED VEIL

DR. PETER M. HAYDEN said that M. M., a white man, aged 64 years, was first seen in the Billings Eye Clinic in December, 1953, with the complaint of "cobwebs" over the left eye of eight months' duration. There was a history of hypertension of eight years' known duration; no previous ocular difficulties were given. He is currently being followed in the cardiovascular clinic for hypertension of about 200/100 mm. Hg. Blood sugar was within normal limits.

Vision was: R.E., 20/50, corrected to 20/15; L.E., 20/200, corrected to 20/20. Intraocular pressure (Schiotz) was 21.5 mm. Hg. R.E., 12.0 mm. Hg, L.E.

Ophthalmoscopic examination indicated moderate attenuation and marked variations of caliber of the arterioles. In the left eye a fan-shaped, richly vascularized membrane extended about six diopters into the vitreous; its retinal line of origin beginning three disc diameters superotemporal to the disc and extending one disc diameter inferonasally, crossing the disc from the 1- to 5-o'clock position.

The etiology of this vascularized veil is unknown, although it probably represents either a congenital defect or an organized vitreous hemorrhage. The systemic hypertension with rather marked retinal arteriolar changes, together with the recent onset of

symptoms, lend weight to the latter possibility.

*Discussion.* DR. FRANK W. NEWELL: Vascular veils within the vitreous occur as a cardinal sign of previous occlusion, usually venous, but occasionally arterial. It is seen rarely in glaucoma, following optic neuritis, and rarely accompanies endarteritis. Its occurrence in diabetes, arteriosclerosis, and other senile conditions is usually indicative of vascular occlusion rather than a complication of the disease.

It may occur as a congenital defect, in which case it is bilateral, usually seen in young individuals, and usually associated with marked loss of vision. The history of hypertension in this man lends weight to the viewpoint that this neovascularization indicates some previous venous difficulty, although a definite area of occlusion cannot now be demonstrated. In the absence of further occlusion, such a veil is probably perfectly compatible with good vision for many years.

### PENETRATING WOUND OF CORNEA AND LENS

DR. SHELDON ZINN presented E. W., a white man, aged 23 years, first seen in Billings Hospital emergency clinic on October 25, 1953, with a complaint of foreign body in the right eye, which followed working with a hammer and chisel earlier in the same day. He was seen in an outside clinic shortly after the accident, where he was told that the foreign body had been successfully removed. The eye remained somewhat painful.

Vision was: R.E., 20/30-3; L.E., 20/20. There was minimal injection of the right eye.

Slitlamp examination showed a small sealed perforated wound of the cornea; a lenticular wound was present behind and corresponding to the corneal wound. Fundus

examination showed a small glistening body lying in the retinal tissue in the inferior temporal quadrant, about seven disc diameters from the disc. Vitreous hemorrhage was noted along the path of the foreign body from the lens to the retina; the remaining vitreous was clear. Perimetric arc localization placed the foreign body at 17 mm. from the limbus at the 8-o'clock position.

Sweet's localization on the day of admission presented a tiny metallic foreign body 20 mm. back of the center of the cornea, eight mm. below the horizontal plane and two mm. to temporal side of vertical plane either in or posterior to the sclera. On the following day, after local anesthesia and exposure of the globe, a small needle was placed in the sclera and X-ray studies were made, using dental films. These films located accurately the foreign body with reference to the needle, and it was removed without difficulty through a small scleral incision.

The case is presented because of the interesting circumstance of a penetrating wound through the lens with minimal lenticular damage and the retention of good vision.

*Discussion.* DR. ORVILLE GORDON mentioned two such cases seen in the last two years and so far there has been no change. Both are industrial cases, and the patients are anxious to know whether cataract will develop.

DR. FRANK W. NEWELL said it was hoped that nothing would occur to complicate this case. In most of the standard texts on ophthalmology we read that a penetrating wound of the lens will cause a cataract which will eventually fully occupy the lens; yet the same texts tell us that in a rabbit's eye a penetrating wound is not followed by a cataract. If the injury to the lens capsule is small enough, there may be a localized subcapsular opacity and, with healing, this may be the full extent of the injury.

In localizing the foreign body in this case, a small needle was placed into the area of the sclera nearest the site of localization of

the foreign body. Dental film was then cut to size and placed behind the conjunctiva and Tenon's capsule, and pictures were made with a portable X-ray machine at the operating table; then the foreign body was localized with reference to the two needles.

The scleral incision, fortunately, was made right over the site of the foreign body. Prior to this, the area was surrounded with diathermy punctures, and it is hoped that there will be no development of cataract or retinal detachment.

DR. MAURICE PEARLMAN remarked that, in his experience, the Berman localizer entirely eliminates the need for such X-ray studies during the operation.

#### GLAUCOMA AS COMPLICATION OF OSTEITIS DEFORMANS (Paget's disease)

DR. WILLIAM M. JONES presented G. D., a 60-year-old Negro, who has been followed in Provident Hospital since 1948. She first complained of poor vision for both distance and near and no other positive symptoms. Both eyes disclosed normal tension; lenses and media were clear except for many fine glistening particles in the vitreous known as synchysis scintillans. Vision was corrected in each eye to 2/25 with a plus sphere and a somewhat stronger cylinder.

In February, 1950, she complained of pain in both eyes and blurring of vision. Tension (Schiotz) was found to be: R.E., 35 mm. Hg, L.E. 65 mm. Hg. Under treatment with miotics, heroic at first, the tension dropped to: R.E., 22 mm. Hg; L.E., 21 mm. Hg, and remained normal. She complained of photophobia and marked ciliary tenderness. The eyes remained pale with no signs of inflammation. It was noted that the tenderness involved the entire left side of the face as well as the region around both eyes.

X-ray films revealed generalized hyperostosis of the skull table, calcification of the falx cerebri and in the region of the pineal, clouding of the left maxillary sinus, and sclerosis more extensive in the left than the right orbital foramen. Nothing



seems to relieve the tenderness. The fields, which were constricted 10 to 15 degrees, have remained the same. Vision has remained the same. There is involvement of the knees and fingers as a result of the disease. It is hoped that the tension will continue to respond to miotics, inasmuch as previous experience has shown that patients with Paget's disease do not respond well to surgery.

*Discussion.* DR. FRANK W. NEWELL said that any hyperostosis of the skull gives rise to a serious problem. We occasionally see a localized area of hyperostosis or benign osteoma which may involve various sinuses. Its occurrence in the frontal sinus with penetration intracranially causing mental symptoms gives rise to Morgagni's syndrome. Hyperostosis may occur as part of a generalized thickening of leontiasis ossea in which there is a marked thickening of all the bones of the skull with formation of a lionlike facies which gives the name to the process.

With any hyperostosis involving the skull it is most important to exclude that associated with meningioma. Histologically a meningioma is a benign tumor that responds very favorably to surgical treatment. We must therefore do everything in our power to exclude meningioma before we decide that the hyperostosis is a noncorrectible condition.

It seems possible that with this bony proliferation within the skull, the fifth nerve is involved, giving rise to the neuralgic pain. Possibly a section of the descending root of the fifth nerve might relieve the symptoms, but that is a question for the neurologist and neurosurgeon to decide.

Richard C. Gamble,  
*Recording Secretary.*

---

OPHTHALMOLOGICAL  
SOCIETY OF  
MADRID

April 22, 1954

SYNCHYSIS OF VITREOUS

DR. SUNER SANCHIS described a case with snowlike sparkling of the vitreous body. This is to be distinguished from synchysis scintillans since it can occur without being followed by the latter. After discussing isolated synchysis, he explained the two principal groups which combine to produce the phenomenon of sparkling, touching upon the clinical and chemical nature of the corpuscles. He gave a historical resume of the cases of snowy scintillating bodies, mentioning the case he presented at a previous meeting of the society. Finally, he outlined the most important pathogenic theories and methods of treatment as given by various authors.

*Discussion.* DR. ARJONA said that the glittering synchysis, like all lipodoses of which it forms one facet, is intimately bound up with a process in which there is deficient local oxidation. This is facilitated by an excess of cholesterol in the blood and by local pathologic disturbances which cause a precipitation of the cholesterol.

When it is an isolated sparkling synchysis one must always think that there is something wrong in the retina or uvea. He cited two cases in which the vitreous could not be seen because of lesions in the plane of the pupil which prevented such examination.

In both cases, in which one eye was completely blind because of an old trauma and was in a degenerated but not atrophic condition, there could be seen large formations of cholesterol suspended in the anterior chamber, of such quantity that they gave to the cornea a beautiful brilliant metallic color.

In one of them the amount of cholesterol was so great that it formed a sediment at the bottom of the anterior chamber, forming a pseudohypopyon. Removing the aqueous humor with all its contents by keratotomy

was ineffective, since after some 24 hours the condition recurred as before.

#### POSTSURGICAL CYST OF IRIS

DR. HERNANDEZ BENITO presented the case of a 60-year-old woman operated for cataract in June, 1952, who in January, 1954, had a serous cyst of the iris. Mackenzie (1830) first described a cyst of the iris and taught its possible traumatic origin. Hulke described 19 cases. Rothmund, in 1871, described 36 more cases. Specific reference was made to the statistics published by Villard and Dejean. The various classifications of cysts were reviewed down to the work of Duke-Elder, which is almost complete. There is no manifest categorical separation of cysts because the etiology is still unknown.

Turning to cysts caused by trauma, Dr. Hernandez Benito divided them into two classical divisions, the pearly (more solid contents) and the serous. He outlined morphologic, topographic, and anatomic-pathologic studies of them. He also gave their clinical evolution and the complications that may arise.

To study their pathogenesis he discussed the experiences of Dosrenal, Golriezher, Schweninger, and particularly those of Masse. He also mentioned the works of Dellaporta and Shigeta. To explain the condition he accepted the teaching of Buhl-Rothmund. He followed up with the differential diagnosis between pearly cysts and serous cysts, as well as between other processes which may have their seat in the iris. With reference to treatment he referred to the work of many authors and finally to the work of Professor Carreras which appeared in the *Archives of the Spanish-American Society* in December, 1952.

**Discussion.** DR. ARJONA said that, with reference to cysts which occur after an operation in which there was an iridectomy, of which he recently had two cases, one must think that their production is caused by the

incarceration of epithelial cells in the stroma of the iris. These by their proliferation give rise to cystic formation.

DR. MARIN AMAT agreed with Dr. Arjona with reference to the epithelial cells spread in the anterior chamber. The epithelial invasion of the anterior chamber can take place by a perforating injury to the cornea, and especially after an operation for cataract, although it is an exceptional case. It occurs when, in the postoperative condition, the epithelium from the borders of the wound proliferates behind the cornea and in front of the iris, covering the latter including the pupillary region. Thus a cystic cavity is formed, complicated by glaucoma which does not respond to any therapeutic measures, ending finally in enucleation of the eye.

Joseph I. Pascal,

Translator.

### MEMPHIS EYE, EAR, NOSE, AND THROAT SOCIETY

#### INTRAOCULAR NEMATODE INFECTION

DR. J. WESLEY MCKINNEY reported the case of R. L. P., aged four years, who was first seen on December 13, 1949. The mother had noticed that for the past year the left eye had turned out. The child has always been healthy although of a nervous disposition. The child was born full-term at the end of a normal pregnancy. Labor was normal except that an injury to the left eye by the forceps was suspected. No details were available.

Examination revealed vision by illiterate chart to be: O.D., 20/20; O.S., 20/400. The left eye was divergent 10 degrees for distance and near. With dilated pupils, the right eye was normal, but the left fundus showed a dense white atrophic plaque between the disc and macula.

In March, 1952, approximately two years later, the child now being six years old, the condition was found to be the same except

that the vision in the left eye was now reduced to moving objects.

On December 18, 1952, three years after the first visit, the child was brought in with the history that something white had been seen in the pupil for three months. There had been no illness or other eye symptoms since the last examination. At this time the right eye was normal, but there was a white mass or membrane tightly apposed to the posterior surface of the lens. A few fine blood vessels could be seen on the surface of the mass, and there were a few small hemorrhages on the posterior surface of the lens. Transillumination was good. Tension was normal.

Because of the fact that this retrolental mass had not been present on previous examinations, retinoblastoma could not be ruled out. Consequently, an enucleation was performed on December 27, 1952.

The report from the Armed Forces Institute of Pathology gave the diagnosis of chronic endogenous enophthalmitis, etiology undetermined, subretinal hemorrhage, retinal detachment, and early complicated cataract. This report was received in June, 1953. A subsequent report, after serial sections had been made, revealed a degenerated nematode larva in the inflammatory cyclitic membrane.

After receiving this report the parents were contacted. They did not know of any indication of helminthiasis and were not disposed to have the child examined for the condition.

#### RETENTION CYST CONTAINING SUTURE MATERIAL

DR. CHARLES KING presented the case of Mr. W. S. H., aged 46 years, first seen on January 22, 1952, with history of a red, tender right eye for 24 hours. There was a moderate conjunctivitis, with edema of the lower half of the bulbar conjunctiva. Small subconjunctival hemorrhages were scattered over the entire globe. Cornea was clear. No foreign body was found. No preauricular adenopathy. Secretions from eye were min-

imal. Treatment with aureomycin ointment, four times daily, and cortisone drops, three times daily, was prescribed.

On January 28, 1952 (six days later), there was considerable edema and swelling of the temporal aspect of the bulbar conjunctiva. A small ulcer at the limbus, 9-o'clock position, was treated with trichloroacetic acid. Terramycin ointment was prescribed for use three times daily and cortisone drops before retiring were advised.

On February 18, 1952, the patient stated that the inflammation had cleared rapidly but he had noticed a small swelling on the eyeball for two days. There was a rounded mass beneath the conjunctiva, temporal aspect, not tender, and fixed to the episcleral structures. It was about the size of a small pea.

At operation on February 22, 1952, the cyst was found to be lying on the tendon of the external rectus muscle. Very careful dissection was done to remove its attachment to the muscle tendon. Just before completely freeing the cyst, it was inadvertently nicked with the scissors and viscid grayish fluid flowed out, followed by a thin wormlike structure. The excision was completed and the conjunctiva closed with 6-0 silk. Post-operative course was not eventful.

The wormlike structure proved to be two inches of plain catgut suture. The patient had been living with foster parents since the age of six years, and neither he nor his parents had any recollection of any ocular surgery having been done.

If the facts are accepted on their face value, it can be assumed that ocular surgery had been done on the patient more than 40 years ago, and that conjunctival infection invaded a retention cyst containing suture material, and this in turn made the presence of the cyst known. It may also be concluded that not all so-called absorbable suture is actually completely absorbed by the ocular tissues.

A specimen of the cyst and suture was shown.

## GONORRHEAL CONJUNCTIVITIS

DR. H. T. McIVER reported the case of D. H., a 40-year-old Negress who was seen on August 18, 1953, with the history of having "sand" in her eyes for eight days, of the eyes being extremely painful and of pouring pus. The patient had experienced a low-grade fever for seven days.

General history and physical examinations revealed the patient to have a purulent cervical discharge and pelvic inflammatory disease. Past history failed to reveal any ocular infections, injuries, or operations.

Physical examination revealed both eyes to be involved in a violent acute inflammatory process. The lids were so tense, brawny, and boardlike that the patient was unable to open them. A yellow purulent discharge trickled almost continuously from between the lids. This discharge seemed to form as fast as one could cleanse it.

The conjunctiva was bright-red, velvety, and so chemotic that the cornea seemed to lie in a deep crater. The preauricular glands were palpable and definitely tender. The corneas, which were difficult to visualize, were involved in a generalized haze, dullness, and disabling opacity. Two gray spots were seen in the left eye. These seemed to coalesce and form deep ulcers. Several smaller marginal ulcers were present. Increased corneal vascularization was evident bilaterally.

Vision in each eye was counting fingers at one foot.

A Gram stain was made from the purulent discharge from both the cervix and from the conjunctiva. Numerous gram-negative intracellular diplococci morphologically resembling gonococcus were found in each. The pathology found on each slide was identical.

The patient was given sulfa and penicillin systemically in heavy dosages. Copious amounts of boric-acid solution were used as often as necessary to prevent pooling of the purulent secretion. This was followed by the instillation of penicillin drops (2,500 u./1.0 cc.) every one to two hours. Atropine

(one percent) drops were given three times daily. Empirin with codeine and sedatives were given for symptomatic relief.

Cessation of the discharge was prompt within 24 hours. The chemosis and the lid involvement rapidly subsided within three to four days. In four to five days the corneal dullness and haze subsided to such an extent that the vision was 20/400, O.U. The patient was given local cortisone drops at the beginning of the 10th day with the hope of decreasing the fibroblastic and proliferative changes. At the end of 14 days the patient was comfortable and was dismissed on local cortisone therapy only. Vision in each eye at this time was 20/200.

*Discussion.* This case of bilateral gonorrheal conjunctivitis in the adult is presented because of the relative infrequency with which one encounters this disease, particularly in private practice, in this era of antibiotics. It should serve as an excellent teaching case for those who were trained just barely in the preantibiotic era and for those who have been trained solely in the antibiotic era. Perhaps it may serve to refresh the memories of senior practitioners, reminding them of what they formerly encountered with moderate frequency.

This case clearly demonstrates how important it is to know exactly the causative organism before beginning definite treatment. The secretion and epithelial scrapings should be studied by Gram's stain in every case of severe acute conjunctivitis. Also definitive treatment should be instituted at the very onset of this disease.

Although, formerly, irreversible changes occurred in gonorrheal conjunctivitis and the eyes became hopelessly blind, now with adequate and correct antibiotic therapy, certain of these changes may be reversed and some vision can be preserved. However, if the case is not seen until corneal haze is present, there is no prospect of saving good vision.

The therapy has changed in recent years, since the advent of antibiotics, to such an ex-



tent that gonorrheal conjunctivitis no longer presents a burdensome nursing routine of eye irrigations every 15 minutes day and night. Penicillin, aureomycin, and terramycin, are the drugs of choice in this condition. Because of the severity of the infection and because of the presence of a gonorrheal infection elsewhere in the body, both local and systemic therapy are indicated.

Infiltration of the cornea is the most serious complication of this disease, particularly when the chemosis is marked. Therefore, in treating gonorrheal conjunctivitis, all efforts should be directed toward prevention of corneal complications.

Adequate prophylaxis both as to the genital gonorrheal infection and the gonorrheal conjunctivitis should continue to be given as it has been within recent years. Finally, all patients who have a gonorrheal discharge from the genitals should be warned of the danger of contaminating the eyes by the secretion.

#### GLAUCOMA IN ONE-EYED YOUTH

DR. ALICE R. DEUTSCH presented the case of H. R., Jr., a 17-year-old Negro. He has been under observation ever since November 4, 1950. At that time he came to the office because of a headache. His general health was good and his family history unessential. The left eye had to be removed because of recurrent inflammation following a perforating injury which occurred several years previously.

The right eye was normal in its anterior and posterior segment. The intraocular pressure was 30 mm. Hg (Schiotz). The peripheral field as tested with a target of 1.5/330 was normal. The central field as tested with a target of 1/1,000 was also normal. He saw 20/20 with a mild myopic correction. The range of accommodation equalled 7.0D.

The intraocular pressure was checked several times a day and varied between 28 and 32 mm. Hg. The drinking test increased the tension from 28 to 34 mm. Hg. Homatropine did not change the tension. Gonioscopy

showed a deep anterior chamber with no abnormalities in the chamber angle. Tonography was not done. Physical examination was negative.

The boy was put on pilocarpine (one percent, twice a day) which lowered the tension to 22 mm. Hg. He was checked three to four times a year and once a year the pilocarpine was discontinued for four days, which always caused the tension to increase to 28 to 32 mm. Hg. No change was noticeable in his visual acuity but he now needs a higher myopic correction. The central field is unchanged. Homatropine was used again in July, 1951, and did not change the tension.

The boy is now 17 years old and will go to college next year. He is presented for consultation with the question: Is it now safe for him to go away to college, continuing to use the one-percent pilocarpine, and with a letter to a specialist setting forth his history, and the request that he be kept under close observation. Any suggestions would be of value.

#### CONGENITAL ICHTHYOSIS

DR. OSCAR DAHLENE, JR., presented a 20-year-old white woman afflicted with a severe case of congenital ichthyosis of the skin involving the face and lids in the process.

The patient presented herself at the John Gaston clinics with severe ectropion of both lower lids and multiple chalazions of all lids. The facial skin was very tense and inelastic, pulling down the lids. The tarsal plates were thick, and the conjunctiva was chronically inflamed and thickened.

Before attempting to correct the ectropion, seven large chalazions were removed from the right lids, and five from the left lids, in two sittings. This thinned the lids considerably. Next the lids were brought into correct position by placing a five-mm. wide graft of postauricular skin in the lower lids, extending from canthus to canthus, tapered at the ends, and temporary tarsorrhaphy to hold the position. Good correction has resulted.

Ichthyosis is a congenital abnormality of



the skin of unknown etiology with hyperkeratosis of the horny layers of the skin and an absence of the secretion of the sweat and sebaceous glands of the skin. It is usually present at birth or shortly after. There are no inflammatory changes, but the sweat glands are aplastic, the sebaceous glands atrophic, and there is loss of the granular layer of the epidermis with hyperkeratosis.

As a rule, the face and lids are affected only in the more severe cases, with fine scales collecting around the base of the cilia and interfering with development so that the lashes are often lost. Ectropion and lagophthalmos, with danger to the cornea, may develop, with multiple chalazions and exposure changes of the conjunctiva.

The disease may be inherited as either a dominant or sex-linked character. Treatment is only supportive, with administration of vitamins and hormones of little or no value. Ectropion is treated by skin grafting, tarsorrhaphy, and excision of chalazions.

#### TUBERCULOUS UVEITIS

DR. FRED WALLACE presented the case of a white man, aged 40 years, who was first seen four days after his right eye became sore. Examination revealed normal vision in each eye with an acute iritis of his right eye with moderate flare and many small keratic precipitates. Ocular tension was elevated to 27 mm. Hg. (Schiotz) in this eye, with hyperemia of the disc and marked retinal artery pulsation being visible at the disc. Tension in his left eye was 14 mm. Hg. Laboratory tests, dental, and physical examinations were normal. Skin tuberculin for 1:10,000 was positive.

Local cortisone, atropine, and heat was prescribed and examination in 48 hours revealed no appreciable change. The pupil was well dilated and the tension still elevated.

Oral hydrocortisone was begun and in two days the characteristics of the keratic precipitates had changed to a larger type, greasy and approaching but not typical of the mutton-fat variety. The aqueous ray,

cells, and keratic precipitates were worse. Tension was 32 mm. Hg in this eye. It was decided that this was a case of granulomatous iritis, perhaps tuberculous.

The oral dihydrocortisone was discontinued and the same local medication was continued. Dystricin intramuscularly (1.0 gm. every three days) and 8.0 gm. of PAS daily were begun. In four days there was a marked improvement. In eight days the keratic precipitates were reduced in number, the flare was less. In two weeks all inflammatory signs had disappeared and tension was 14 mm. Hg.

This case appeared to be one that initially resembled a serous iritis. Treatment with local and systemic hydrocortisone only made it worse. When the keratic precipitates changed to those resembling a granulomatous type, the hydrocortisone was stopped and, on systemic streptomycin/dihydrostreptomycin and PAS the iritis disappeared. The case demonstrates, as has been pointed out by Dr. Alan C. Woods and others, that cortisone or similar-acting hormones make tuberculous uveitis worse and are contraindicated.

Daniel F. Fisher,  
*Recording secretary.*

#### YALE UNIVERSITY CLINICAL CONFERENCE

January 29, 1954

DR. R. M. FASANELLA, *presiding*

#### PROBLEMS OF REFRACTION

DR. ALFRED COWAN, professor of ophthalmology, University of Pennsylvania Graduate School of Medicine, was the guest speaker. He discussed problems of refraction.

#### APHAKIA

Would you comment on your medical preference in handling cases of aphakia, as to whether the change in prescription power should automatically be computed and produced by the doctor or optician.

*Answer.* Trial lenses do not conform to the usual deeply curved spectacle lens. Put the final prescription in the trial frame in the lensometer to get the vertex refraction, of the sphere especially. Write "Grind as written."

Do you think operating both eyes for cataracts is optically sound or should it be avoided?

*Answer.* I do not feel that a second cataract extraction should be done on an elderly patient with a successful operation on the first eye. For most things, one eye is as good as two. I do not believe patients with bilateral aphakia ever get good binocular vision.

#### MYOPIA

What are the present concepts concerning full correction of myopia in youth?

*Answer.* I think there should be a full correction because every patient is entitled to the best acuity possible for him. However, I do not think it has any therapeutic effect.

Do you believe in eye exercises for myopia?

*Answer.* You cannot change the degree of ametropia with exercises. You may be able to train the visual response somewhat. Two people, each with one diopter of myopia, may get along very differently, and subjective estimates of visual improvement are unreliable as evidence of a change in the degree of ametropia.

#### HEADACHES AND GLASSES

In general how many headaches are due to refractive error as compared to other causes?

*Answer.* Ask whether the headaches are connected directly with the work they do. The therapeutic test only is important, however.

Do you think that such a small correction as 0.5D. sph. or 0.5D. cyl. when no increase in visual acuity occurs is helpful to some adults?

*Answer.* A 0.5D. sph. is of no use in any

young patient with good accommodation. However, 0.5D. of astigmatism can cause real asthenopia, and correction of the astigmatism may be helpful.

What is the present status of aniseikonic corrections in regard to correcting symptoms supposedly due to aniseikonia?

*Answer.* There is not as much enthusiasm now in regard to these problems as formerly. Uncorrected lenses may produce some aniseikonia. Even "corrected" lenses are not good for some purposes. Lenses would be better if they all had similar minus base curves, but this is not practical for stock lenses. Present corrected lenses are in several series according to strength, with different base curves for each series. It is possible with a small degree of anisometropia to have large differences in back curves if one lens happens to fall at the end of one series, and the other at the beginning of the next series.

#### AIDS AND REFINEMENTS OF REFRACTION

What are the advantages and disadvantages of using telebinocular for taking visual acuities?

*Answer.* It is useful where you have laymen making the tests, or haven't enough distance for Snellen tests, but it is not good from the standpoint of the ophthalmologist.

Should the dominant eye be made to see better or is it as well to make both eyes see equally well?

*Answer.* I make both eyes see equally well. Do you use telescopic lenses often?

*Answer.* Very, very seldom. The newer telescopic lenses are still only telescopic lenses, and they all give a relatively small field.

What are the advantages and disadvantages of the streak retinoscope over the regular retinoscope?

*Answer.* I still use the ordinary reflecting retinoscope.

#### CONTACT LENSES

Do you prescribe contact lenses?

*Answer.* Occasionally.

What is the value of contact lenses in unilateral aphakia?

*Answer.* It is no good optically especially in people with good accommodation. There is a 10-percent difference in image size, and with accommodation, the vision must blur at different distances, even with a 2.75D. add for near. I think the patient doesn't need good binocular single vision.

#### VERTICAL IMBALANCE AND PRISMS

We know that there may be an association of refractive error with esophoria, esotropia, and exotropia—is there any association of refractive errors with vertical phorias?

*Answer.* I don't think so. I correct it always—as fully as I can without overcorrection. Occasionally, people with six, seven, or eight prism diopters of hyperphoria are more comfortable without correction. Here again, it is not always necessary to give binocular vision as long as the patient is comfortable.

#### ASTIGMATISM

If a 40-year-old person who had never worn glasses came to you with a vision of say 20/70 in each eye and showed an astigmatism say of 6.0D. cyl. in each eye that could be corrected to say 20/30 or better, how would you handle it?

*Answer.* Be very careful. A trial wearing of the correction for a while in the office may be helpful. You may cut the strength in half. Never force it on them.

What is the technique of the near-point testing for astigmatism?

*Answer.* I do not use it. I feel dynamic skiascopy is also very unsatisfactory.

What should a balance lens be?

*Answer.* Just a lens that looks like the other; and the cheapest one.

#### GENERAL DISCUSSION

**DR. LOVEKIN:** How would you feel about bilateral surgery in a patient, aged 40 to 50 years, with bilateral cataracts?

**DR. COWAN:** It might be better cosmetically, but that's all.

**DR. W. GLASS:** What do you think of the Rodenstock refractionometer?

**DR. COWAN:** I think it is good, but why spend \$1,000.00 for a retinoscope? It gives good results under cycloplegia but, without cycloplegia, it has to be checked anyway.

**DR. WIES:** In testing vertical phorias, do you have the patient look down to check them at the reading distance?

**DR. COWAN:** Yes, and give them the least prism of several readings if the findings are variable.

**DR. KAPLAN:** Do you patch the good eye for amblyopia when there is a marked difference in refractive error of the two eyes, and, if so, how long?

**DR. COWAN:** Yes. The vision seldom comes up to the other eye. I would persist in patching for three to four months, and if no response, wait a while, then perhaps try again.

**DR. PATTERSON:** How would you treat a patient aged 70 years in whom you find a two diopter change in one eye?

**DR. COWAN:** Give the correction. It may be due to a change in the crystalline lens. It is also common to find more plus required in presbyopes.

**DR. WONG:** In accommodative esotropia, do you prescribe the fullest hyperopic correction?

**DR. COWAN:** Yes.

**DR. B. ALLEN:** In a presbyope with astigmatism, should you incorporate the astigmatic correction in a single vision reading glass if he wears no distance glasses?

**DR. COWAN:** Yes.

**DR. FASANELLA:** Would you give us your opinion on tinted lenses?

**DR. COWAN:** The light shades are absolutely useless. When the lighting in our environment varies frequently from three to 10,000 foot-candles, a two to 10-percent decrease means nothing. You can't cure true glare with any lens. In regard to nonreflection coatings: these help some by diminishing reflections 20 percent, but it does make the lens less transparent. Some people are

annoyed with small ghost-light reflections. These are due to internal reflections from the lens surfaces, and coating reduces, but never eliminates them. The patient must be urged to disregard these reflections.

William I. Glass,  
*Secretary.*

NEW YORK SOCIETY  
FOR CLINICAL  
OPHTHALMOLOGY

March 1, 1954

DR. BERNARD FREAD, *President*

MANAGEMENT OF FOREIGN BODIES IN THE  
VITREOUS

DR. HARVEY E. THORPE said an accurate and complete diagnosis is important in every case of intraocular foreign body. This should be based on an adequate detailed history of injury and on a careful description of the specific work engaged in while injured. The tools employed at the time of accident and the surfaces of colliding metals, which might have caused the injury, should be examined. Foreign particles from the skin neighboring to the eye due to explosions may give a clue to the nature of the intraocular foreign body.

Complete routine clinical examination of both eyes, including visual acuity, biomicroscopy, transillumination, and estimation of intraocular pressure, should be done. One must be on the lookout for evidence of foreign-body presence, such as perforations of the cornea, sclera, iris, lens, retina, and so forth. Other evidence of intraocular foreign body, such as siderosis or chalcosis, should also be looked for. Patients suffering from recurrent uveitis or iritis of vague etiology should have the presence of an intraocular foreign body ruled out.

Every suspicious ocular injury should have roentgenologic examination. The Sweet, Comberg, and Vogt methods of intraocular foreign-body localization are a great help when they are performed accurately.

Dr. Thorpe's plastic localizing shell for

the Comberg technique can be used in fresh injury cases. It can be sterilized with 1:1,000 Zephiran. It has a small corneal venthole which prevents its being held against the globe by suction, thus making its removal after examination easy. This contact lens can readily be sutured to the globe when necessary.

Air injection in Tenon's space is a very useful technique for differentiation of double perforation of the globe in doubtful cases. It is performed by grasping the conjunctiva and Tenon's capsule between two adjoining rectus muscles in the quadrant in which the foreign body is located and injecting six to eight cc. of air through a 27-gauge hypodermic needle. Escape of air beneath the conjunctiva is prevented by pinching the point of perforation of Tenon's capsule for several moments after withdrawing of the air injection needle. The Berman locator has proven to be a valuable aid for localizing magnetic foreign bodies. It also helps to differentiate these from the nonmagnetic particles.

Chemically inert intraocular splinters need not be removed unless they are large or cause irritation. This includes glass, coal, lead, and the precious metals. A diagrammatic sketch of the site of perforation, of the trajectory, and of the position of the foreign body, as well as other data, should be recorded at the time of examination. This is important for later reference.

When first-aid is rendered in these cases, manipulation of the globe should be avoided. A sterile protective dressing should be applied and an ophthalmologist should be consulted within the course of one or two hours.

—Protective measures must be taken against infection. Antibiotics in large doses, sulfonamides, prompt aseptic reparative surgery, foreign-protein therapy, and administration of tetanus and gas-bacillus antitoxin are important steps in helping to save an eye harboring an intraocular foreign body. Such drugs should be administered with great care to allergic or sensitive individuals.



In the operating room one should have available nonmagnetic instruments—a giant and a hand electromagnet, a source of direct current for the electromagnets, a Berman locator, a diathermy current apparatus, an ophthalmoscope, and other pertinent instruments. Either local or general anesthesia may be used. The average patient with an intraocular foreign body prefers pentothal anesthesia. Preoperative sedation is advisable. The barbiturates such as pentobarbital or sodium amytal are preferred in preoperative preparation.

The removal of an intraocular foreign body from the vitreous can be approached by the anterior route or by the transscleral approach. By the anterior technique, the pupil must be fully dilated. This technique is limited to foreign bodies up to 2.5 mm. long by 1.0 mm. in thickness. One must be careful to avoid injury to the crystalline lens and to avoid entangling the foreign body in the ciliary processes. The Haab giant magnet, the Lancaster giant magnet, the Mallinger magnet, and others, may be used for this technique.

The foreign body is brought into the anterior chamber around the equator of the lens. It is dropped on the iris. It is then removed through a peripheral corneal incision with the aid of a hand magnet. As a rule, it is preferable to remove a foreign body through a keratome incision rather than through its wound of entry.

Both large and small foreign bodies in the vitreous can readily be delivered through an incision of the flap-door type located over the pars plana of the ciliary body. Such an incision is made in the proper quadrant overlying the foreign body at a distance of five to six mm. behind the limbus and in front of the ora serrata. If a foreign body is wedged or attached to the retina, it is best brought out transsclerally at that point. The incision at the point of delivery should be placed with the aid of the Berman locator, and can be surrounded with surface diathermy previous to completion. Preplaced

sutures can also be used and are extremely helpful in prevention of vitreous loss. The Lancaster and Hirschberg hand magnets are useful for this purpose.

Nonmagnetic foreign bodies must be seen to be grasped. An intravitreal foreign body visible with the ophthalmoscope can readily be brought out through a scleral incision with special type forceps. A flap-door incision can be made in the sclera by surface diathermy. The foreign body can then be visualized in the vitreous with the aid of a transilluminator on the opposite side of the globe or directed into the pupil zone.

In other instances where the foreign body is deep in the vitreous and the transilluminator and ophthalmoscopic technique are not available, the ophthalmic endoscope should be used. It can be applied in cases where the vitreous is not filled with blood or exudate. The lamp of the endoscope should not be overvoltaged to avoid heat coagulation and clouding of the vitreous. The objective lens of the endoscope which comes in contact with the surface of the vitreous should be dipped into a wetting solution such as 1:5,000 Zephiran. The instrument should not be thrust into the vitreous chamber, but held against the surface of the vitreous body.

Diagnostic procedures, including X-ray examinations, should be performed promptly, so that the odd intraocular foreign body may be removed within the first 48 hours. Surgical procedure should not be performed before all necessary information is available. Intraocular foreign bodies often carry infection into the eye, and such infection cannot be stopped until the particle is removed. Organized hemorrhage and cicatrization make removal of a foreign body difficult.

In any case in which there has been a perforation of the retina, either on entry or exit, proper diathermy application should be made to the sclera over the retinal hole. The patient should be treated postoperatively like any retinal detachment case. This includes the use of stenopeic goggles.

Cortisone and ACTH are useful adjuncts



in allaying severe preoperative inflammation or marked postoperative reaction. Unless contraindicated due to history of psychosis, active peptic ulcer, or tuberculosis, intravenous ACTH may be given in 25-mg. dosage. This is dissolved in 500 cc. dextrose and administered at the rate of 15 drops per minute. This intravenous corticotropin therapy may be repeated for two or three days.

Traumatic cataract is one of the serious complications and is often handled best at a time subsequent to removal of the foreign body. On occasion, the perforation of the crystalline lens does not go on to full cataract formation. The lens is retained and the individual may have rather good vision. Sympathetic ophthalmia is a rare complication, but must always be watched for. The presence of an intraocular foreign body is indicative of a serious penetrating injury to the globe and often portends dire consequences. The prognosis is always guarded. The gravity of such cases depends on the extent of anatomic injury, the character and extent of loss of global content, the amount of visual impairment, the presence of infection, the severity of the inflammation, and the chemical nature of the foreign body, its magnetic properties, its location in the globe and accessibility for extraction, in the presence of such other complications such as traumatic cataract, prolapse of intraocular tissues, hemorrhage, retinal detachment, vitreous bands, and, of course, on the eye's ocular response to therapeutic measures.

*Discussion.* DR. KRAVITZ asked if Dr. Thorpe would proceed to remove an intraocular foreign body in the presence of infection which did not respond readily to antibiotics or other therapy?

Dr. Kravitz went on to say he would like to emphasize the point Dr. Thorpe had made about the use of X-ray studies and that he would also like to ask Dr. Thorpe about another case that he saw.

The gentleman was working when some-

thing went into his eye. However, he made no report. About a month later he stated he could not see. On examination he had a hole in the iris, a wound in the cornea, an opacity of the lens in the lower part, with signs of intraocular foreign body. Two other consultants saw him and they all agreed that this man must have had an intraocular foreign body, but repeated X-ray examinations and dilatation showed no intraocular foreign body.

Dr. Kravitz suspected that the patient must have had something that was removed, but he denied this.

DR. THORPE replied thanking the discussers for their kindness. In reply to Dr. Kravitz, with reference to removal of a foreign body in the presence of infection which did not respond to antibiotics or in which infection developed, it has been my practice to remove it at once. The decision is based on the following reasons:

On a number of occasions foreign bodies were removed and cultured and it was found that the foreign body itself carried a great deal of infection. If it is in the vitreous, unless the foreign body is removed the infection cannot be controlled. Dr. Thorpe said that he would remove the foreign body as soon as he had an opportunity to remove it, especially in the presence of infection and particularly if the foreign body is magnetic. However, one must judge each case for itself.

Error in X-ray localization often happens. Dr. Thorpe found the Berman locator especially helpful. Although there are a number of methods for accurate localization of the foreign body, one must use all his wits, the ophthalmoscope, and so forth. One should have an X-ray examination if in doubt and be on the safe side. If the eye is irritable, make sure and take an X-ray picture. One X-ray film may not be sufficient. The foreign body may be so small, it may not show up.

As to the case that Dr. Kravitz mentioned

with the hole in the iris and cornea, opacity in the lens, and negative to X-ray findings. Dr. Thorpe said he had had a number of cases like that. In some of them, they found that the X-ray film was positive with the Vogt technique. In others, X-ray films were never positive. He had had a foreign body that was not opaque to X ray. At this point Dr. Thorpe referred to a case in which the patient had a perforation of the cornea and hole in the iris. The eye went on to siderosis. There never was a positive X-ray finding. Subsequently, when the eye was enucleated, a piece of porcelain was found—one side had rusted hence it was not opaque to X ray.

#### ANALYSIS OF ECTROPION AND ENTROPION PROCEDURES

DR. ALSTON CALLAHAN said the cause of entropion of the upper lid is usually cicatricial. The strength of the larger tarsus prevents either acute spastic or chronic senile forces from rolling the lid margin in.

In the lower lid, the smaller tarsus is less able to resist acute spastic forces, or the three types of senile changes—spastic, relaxed, or cicatricial, so here the condition develops more frequently. Also, cicatricial entropion of the lower lid will result from diseases in which conjunctival and tarsal contraction is a major feature and from injuries such as molten-metal burns of the inferior fornix. Trichiasis, in which the lashes turn in but the lid margin is in the normal position, is usually caused by cicatrization following a disease process; however, trichiasis and entropion may occur together.

In senile entropion the predominating force may be spastic, relaxed, or cicatricial; it may be from the combination of any two or all three conditions in varying degrees. The role that each plays must be evaluated correctly. With senile atrophy of the orbital fat, a relative enophthalmos occurs and the globe no longer supports the lid. When the lids close in blinking, the lower lid rises and since the upper margin is unsupported by

the globe, it rolls in, allowing hypercontraction of the marginal orbicularis muscle bands of Riolan.

For all lids with senile spastic entropion, except that of the most minimal or extreme degree, my procedure of choice is the technique of crossing the orbicularis fibers and fixing the ends of the strips to the margin. This procedure has been evolved from the original procedures of Wheeler and of Hughes.

When relaxation or lengthening of the lid is the predominating characteristic of senile entropion, Fox's procedure is the method of choice. It is a further refinement of the Butler technique which has been widely used.

The cicatricial type of senile entropion, which has no spastic element, is usually not severe, but the lashes, fine white cilia, and the skin edge of the mucocutaneous junction will abrade the cornea. If the upper lid is not entropic, a three-mm. strip of tarsal conjunctiva can be removed from it near its upper border, and this "donor" defect closed. In the margin of the entropic lid, an incision is made across the mucocutaneous junction and the strip grafted to it. This will place the abrading structures away from the eye so the cornea cannot be damaged.

If the senile entropion of this variety is severe, or if the upper lid is entropic, so that it is not safe to remove a strip of tarsal conjunctiva, one of the procedures for cicatricial entropion after disease or injury is indicated.

*Cicatricial entropion.* Cicatricial entropion occurs after severe conjunctival inflammations, particularly those of a purulent and membranous nature, and trachoma. The last is the most common cause. Here the inturning of the lid margins is aided by the softening of the tarsus and its consequent deformation as a result of the disease process.

Cicatricial entropion also follows chemical and thermal burns, and those injuries which cause contraction. It is more common in the

upper than in the lower lid and is usually bilateral.

The procedure of choice for this condition is the LeGleyze correction.

*Senile ectropion* has been known since ancient times and its frequency is increasing, as are all geriatric problems. It is due to senile changes in the tissues of the lower lid and, depending upon the predominating characteristic, it may be the relaxed, the cicatricial, or the spastic variety. Senile ectropion is usually thought of as the relaxed type; though this is most common, the other two must be clearly differentiated because the surgical repair is entirely different for each.

*Relaxed type.* When atrophic changes have thinned out the skin and muscle so that the lid is lax and hangs forward and downward, successful repair can be accomplished by shortening and strengthening both laminae with the Kuhnt-Szymanowski procedure.

*Cicatricial type.* When contraction of the skin and orbicularis has drawn the lid downward, and shortened and thickened it, successful repair can be achieved by removing the scar tissue, adding skin by free grafts or pedicle flaps, preventing contraction by intermarginal lid adhesions, and elevating and supporting the lid.

My procedure of choice for this is the transfer of a wide double-pedicle flap of the skin and subcutaneous tissues from the upper lid to the lower, described by Stallard as a bridge pedicle-flap procedure. If an area of conjunctiva has become keratinized, it must be resected before the intermarginal lid adhesions are made.

*Spastic type.* If, while the senile relaxation of the skin and lid border is permitting the margin of the lower lid to sag forward and downward, by coincidence spastic contraction of the orbicularis bands along the base of the lid occurs, senile spastic ectropion is inevitable. Successful repair can be accomplished by shortening the lid horizontally and excising part of the spastic orbicularis

bands. The sector of lid to be removed is that where the relaxation is the greatest, and the muscle sector to be removed is that which contracts the most. Usually these two conditions are in the same part of the lid.

The relaxed and cicatricial forms of senile ectropion are usually bilateral but may be more advanced in one lid than in the other. Also, the sagging and downward contraction of the lid is usually greatest at the midpoint but may be more advanced in any sector of the lid. Senile spastic ectropion occurs less often than the other two types and is usually unilateral.

*Discussion.* DR. HUGHES said that Dr. Callahan certainly showed some very nice results. In regard to spastic entropion, some surgeons make a vertical pull on the lower lid for the main part of the mechanical correction of the entropion. Dr. Hughes thought that any operation that uses a vertical band to pull the lower lid down is wrong. The normal muscle in the lid is a horizontal pulling muscle and that muscle should be restored in its normal direction. A downward band tends to limit the motility of the lid and does not restore the normal anatomic relationship.

One thing that Dr. Callahan did not mention is the injection of alcohol for acute cases. Dr. Hughes said he would like to point out that alcohol injection can be done very simply. In almost all cases, it will produce the immediate correction, if done correctly. Alcohol must be given after previous injection of procaine along the surface of tarsus near the lid border. In severe cases one may need to inject the entire tarsal portion of the orbicularis. In a case of short duration, you may get permanent results because the temporary therapeutic result outlasts the cause of the entropion.

DR. MEEK said that he had modified his operation. The medial band is no longer attached to the orbital ridge. The lateral band is attached loosely. In that way, they act as a fulcrum on the tarsus and should prevent it from turning in.

DR. BYRON SMITH said he thought that entropion surgery is about at the stage where glaucoma surgery was 15 years ago. The number of new procedures would indicate that we are still somewhat confused. I hope that within the next five to 10 years, Dr. Callahan can simplify this so that we can all understand it better.

Bernard Kronenberg,  
*Recording Secretary.*

## COLLEGE OF PHYSICIANS OF PHILADELPHIA

### SECTION ON OPHTHALMOLOGY

February 18, 1954

DR. EDMUND B. SPAETH, *Chairman*

#### OPHTHALMOPLEGIAS OF NEURAL ORIGIN

DR. C. WILBUR RUCKER, Mayo Clinic, Rochester, Minnesota: Experience with ophthalmoplegias of neural origin was summarized and several illustrative cases presented. An analysis of 282 cases disclosed that in about 25 percent (67 cases) the cause was not determined. Head injury accounted for another large group (52); of

these, an automobile accident was responsible for over half.

Aneurysm at the circle of Willis was the cause in 31 cases and in two thirds of these the oculomotor was the nerve implicated. In every case of third-nerve paresis due to aneurysm there was some iridoplegia.

Occlusive vascular disease seemed to account for many (54) of the pareses. In this group the patients presented evidence of hypertension or arteriosclerosis, and a few had diabetes. In the majority of these the pupillary reactions were intact and there was a tendency to recovery.

When brain tumor was responsible for ocular palsy the abducens was by far the most frequently affected and was of no localizing value. The third and fourth nerves were involved by tumor infrequently.

Syphilis was responsible for five cases of abducens palsy and one case of paresis of the third and sixth nerves. Its incidence is much lower than it was in former years.

Multiple sclerosis accounted for 11 cases of sixth-nerve paresis. In no case did it affect the third or fourth nerve.

The group of miscellaneous rare cases was not discussed.

William E. Krewson, 3rd,  
*Clerk*

#### OPHTHALMIC MINIATURE

Two years ago, whilst under treatment in Paris (for chronic eczema), his left eye began to protrude, and, to use his own exaggerated expression, "was pushed right out of the head." His Paris doctors proposed an operation, but he was finally cured by Pagenstecher at Wiesbaden by means of large doses of iodide of potassium. The eye, he thinks, receded more than natural, and so also did the left (sic), which had never protruded.

Jonathan Hutchinson  
*Archives of Surgery*, 1:343, 1890.



# AMERICAN JOURNAL OF OPHTHALMOLOGY

*Published Monthly by the Ophthalmic Publishing Company*

## EDITORIAL STAFF

DERRICK VAIL, *Editor-in-Chief*  
700 North Michigan Avenue, Chicago 11  
LAWRENCE T. POST, *Consulting Editor*  
640 South Kingshighway, Saint Louis 10  
BERNARD BECKER  
640 South Kingshighway, Saint Louis 10  
WILLIAM L. BENEDICT  
100 First Avenue Building, Rochester, Minnesota  
FREDERICK C. CORDS  
384 Post Street, San Francisco 8  
SIR STEWART DUKE-ELDER  
63 Harley Street, London, W.1  
EDWIN B. DUNPHY  
243 Charles Street, Boston 14  
F. HERBERT HAESSLER  
561 North 15th Street, Milwaukee 3  
PARKER HEATH  
Sullivan Harbor, Maine  
S. RODMAN IRVINE  
9730 Wilshire Boulevard,  
Beverly Hills, California

JAMES E. LEBENSOHN  
4010 West Madison Street, Chicago 24  
DONALD J. LYLE  
601 Union Trust Building, Cincinnati 2  
WILLIAM A. MANN  
30 North Michigan Avenue, Chicago 2  
P. ROBB McDONALD  
1930 Chestnut Street, Philadelphia 3  
FRANK W. NEWELL  
950 East 59th Street, Chicago 37  
JOHN V. V. NICHOLLS  
1414 Drummond Street, Montreal  
ALGERNON B. REESE  
73 East 71st Street, New York 21  
PHILLIPS THYGESON  
220 Meridian Road,  
San Jose 26, California  
M. URIBE TRONCOSO  
215 West 92nd Street, New York 25  
ALAN C. WOODS  
Johns Hopkins Hospital, Baltimore 5

KATHERINE FERGUSON CHALKLEY, *Manuscript Editor*  
Lake Geneva, Wisconsin

*Directors:* WILLIAM L. BENEDICT, President; FREDERICK C. CORDS, Vice-President; WILLIAM A. MANN, Secretary and Treasurer; F. HERBERT HAESSLER, DERRICK VAIL, ALAN C. WOODS.

*Address original papers,* other scientific communications including correspondence, also books for review to *Dr. Derrick Vail, 700 North Michigan Avenue, Chicago 11, Illinois;* Society Proceedings to *Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Manuscripts should be *original copies,* typed in double space, with wide margins.

Exchange copies of medical journals should be sent to *Dr. F. Herbert Haessler, 561 North 15th Street, Milwaukee 3, Wisconsin.*

*Subscriptions,* application for single copies, notices of changes of address, and communications with reference to advertising should be addressed to the *Manager of Subscriptions and Advertising, 664 North Michigan Avenue, Chicago 11, Illinois.* Copy of advertisements must be sent to the manager by the 15th of the month preceding its appearance.

*Change of address* notice should be received not later than the 15th of the month prior to the issue for which the change is to go into effect. Both old and new addresses should be given.

*Author's proofs* should be corrected and returned within forty-eight hours to the *Manuscript Editor, Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Twenty-five reprints of each article will be supplied to the author without charge. Additional reprints may be obtained from the printer, the George Banta Publishing Company, 450-458 Ahnaip Street, Menasha, Wisconsin, if ordered at the time proofs are returned. But reprints to contain colored plates must be ordered when the article is accepted.

## THE CHEMOTHERAPY OF EYE TUBERCULOSIS

Recent great advances in the chemotherapy of pulmonary tuberculosis are apparently being matched in the chemotherapy of certain extrapulmonary forms of the disease (that is, genito-urinary,<sup>1</sup> miliary-meningeal,<sup>2</sup> lymph node,<sup>3</sup> and intestinal.<sup>4</sup>). The action of combinations of streptomycin, isoniazid, and PAS on M. tuberculosis in the

human host is believed to be almost entirely bacteriostatic. Differences in the proximity and availability of O<sub>2</sub> might well alter the action of these agents on the facultatively aerobic tubercle bacillus in lungs as contrasted to a solid organ with a single blood circulation.

On theoretic grounds, therefore, tuberculosis of the uveal tract should respond to prolonged streptomycin-PAS or isoniazid-



PAS treatment in a manner comparable to the response in renal tuberculosis.

According to A. C. Woods, streptomycin, PAS, and isoniazid are used intermittently, occasionally singly, and for only a few weeks after attainment of the immediate therapeutic objective. Total therapy with anti-tuberculous drugs in these cases is only two to three months. Relapses of uveal tract tuberculosis have occurred within one year in 20 percent of those with a satisfactory early response to short-term treatment.<sup>5</sup> Results of 12 uninterrupted months' streptomycin-PAS and particularly to isoniazid, streptomycin-PAS<sup>7</sup> treatment of renal tuberculosis have been considerably more promising.

Bacteriologic and morphologic confirmation of a diagnosis of eye tuberculosis in the living patient is not available to the ophthalmologist as is the case with renal or pulmonary tuberculosis; nor can the results of chemotherapy be checked bacteriologically as in renal or pulmonary tuberculosis. However, diagnostic criteria for ocular tuberculosis have been established<sup>6</sup> and when, in addition, there is an initial response to specific chemotherapy, may we not draw parallels between renal and pulmonary tuberculosis and treat the eye tuberculosis with long-term and sustained chemotherapy?

The answers to this and related questions are surely more complex than this simple outline of one aspect of the problem would indicate. We encourage, therefore, a round-table discussion of eye tuberculosis, participants to include ophthalmologists with particular interest and experience in eye tuberculosis, at least one urologist with wide experience in treating genito-urinary tuberculosis, and others well acquainted with both the experimental and clinical aspects of the chemotherapy of pulmonary tuberculosis.

Roger S. Mitchell, M.D.

#### REFERENCES

1. Lattimer, J. K., Kohen, H., Lovelock, F., Kenney, M., and Amberson, J. B.: Genito-urinary tuberculosis; Tr. 13th V. A. Conf. on Chemotherapy of Tuberculosis, St. Louis, Feb., 1954, p. 383.
2. Williams, J. H., Jr.: Meningeal and military tuberculosis. Tr. 13th V. A. Conf. on Chemotherapy of Tuberculosis, St. Louis, Feb., 1954, p. 191.
3. Selikoff, I. J., and Friedman, O. H.: Tuberculous peripheral lymphadenitis: Chemotherapy of ambulatory patients. Tr. 13th V. A. Conf. on Chemotherapy of Tuberculosis, St. Louis, Feb., 1954, p. 389.
4. Mitchell, R. S., and Bristol, L. J.: Intestinal tuberculosis: An analysis of 346 cases diagnosed by routine intestinal radiography on 5,529 admissions for pulmonary tuberculosis, 1924-49. *Am. J. Med. Sc.*, **227**:241, 1954.
5. Woods, A. C.: The pathogenesis and treatment of ocular tuberculosis. *Arch. Ophthalm.* **52**:174, 1954.
6. Woods, A. C.: Therapeutic action of streptomycin and promizole in clinical ocular tuberculosis. *Arch. Ophthalm.* **42**:521, 1949.
7. Lattimer, J. K.: Genito-urinary tuberculosis. Tr. 14th V. A. Conf. on Chemotherapy of Tuberculosis, Atlanta, Feb., 1955.

#### WILLS EYE HOSPITAL

##### SEVENTH ANNUAL CLINICAL CONFERENCE

The seventh annual clinical conference of the staff and ex-residents of the Wills Eye Hospital, Philadelphia, was held at the hospital on February 18 and 19, 1955. Attendance exceeded all previous conferences. The official registration was 460.

The guest of honor at the conference was Dr. Leighton F. Appleman, attending surgeon, Wills Eye Hospital, from 1924 to 1939, and consulting surgeon since 1939.

The meeting was opened with a paper evaluating the tuberculin reaction in uveitis. The authors, Dr. Harold A. Hanno and Dr. Philip G. Spaeth, compared the number of positive reactors to PPD in a series of 499 patients with endogenous uveitis to the number of positive reactors in a control group of 197 patients without inflammatory disease of the uveal tract. The results demonstrated that patients with uveitis do not have a higher than normal percentage of positive reactions to tuberculin. They concluded that tuberculosis cannot be considered a very frequent etiologic factor in endogenous uveitis.

Dr. Arthur H. Keeney spoke on the significance and surgery of macular holes in

retinal separation. He pointed out that every punched-out macular lesion is not necessarily a hole in the macula since the lesion may be an intact cyst, a cyst whose inner wall only has ruptured, or normal retinal position may have been retained with perimacular adhesions. The author felt that macular holes rarely occur first in posterior pole separations but more commonly as incidental pathology to incomplete and peripheral breaks, and occasionally as secondary pathology in long-standing separations. Maximum diathermy with 0.5 mm. partial penetrating electrode was recommended to seal complete holes whereas avoidance of incomplete holes at surgery was advised in order to preserve valuable perimacular activity.

Three interesting papers from the Research Department of the hospital, which is under the direction of Dr. Irving H. Leopold, were given at the opening session.

1. Mechanism of Diamox Action (Green, H., Leopold, I. H., Calnan, A. F., Bocher, C., Sawyer, J., Rosenberg, A., and Waters, L.). Adult pigmented rabbits were given Diamox intravenously or subconjunctivally. The carbonic anhydrase activity of the anterior uvea was completely inhibited 30 and 60 minutes after the intravenous injection and 15 minutes after subconjunctival administration. The same treatment did not appreciably lower the intraocular pressure of the normal rabbit eye measured over a period of three hours or significantly lower the bicarbonate ion concentration in the anterior aqueous humor. These workers concluded that carbonic anhydrase activity of the anterior uvea does not control the elaboration or secretion of bicarbonate in the eye and does not regulate the intraocular pressure of the normal rabbit eye. They further felt that the hypotensive action of Diamox upon glaucomatous eyes may be related to some mechanism other than that involving the normal distribution of bicarbonate ion between the blood plasma and aqueous humor.

2. Histochemical staining technique studies were carried out on 30 normal rabbit eyes

and one normal human eye by Dr. P. Carmichael and Dr. I. H. Leopold. They employed the Ritter Olsen stain, the Rinehart Abul-Haj stain, the periodic acid Schiff reaction, and the toluidine blue stain. Areas of normal basement membrane activity were demonstrated in the basement membrane of corneal epithelium, Descemet's membrane, and the fibers of the trabeculum of the filtration angle. The choroidal coats stained as did the internal and external limiting membranes of the retina. Indeed, the entire eye appeared to be lined within by areas of basement membrane. However, eyes with secondary glaucoma showed an increased staining in the area of the ciliary epithelium with a dialyzed iron method.

3. Studies on the steroid content of the aqueous humor by H. Green, I. H. Leopold, and J. Sawyer were reported on. These were performed with 9 $\alpha$ -fluorohydrocortisone in experimental animals and in a variety of external ocular diseases. It was shown that this agent was as effective in its anti-inflammatory properties as hydrocortisone. The 9 $\alpha$ -fluorohydrocortisone was effective in many instances in a weaker concentration than that required for similar antiphlogistic action by hydrocortisone. Penetration studies revealed definite differences for the local acetate and alcohol varieties of cortisone, hydrocortisone, 9 $\alpha$ -fluorohydrocortisone, and hydrocortisone t-butylacetate.

Dr. Walter Fink spoke on the anatomic considerations in vertical muscle surgery.

Dr. Enrique Wudka and Dr. I. H. Leopold gave an interesting report of their studies on experimental glaucoma. Although physiologic seclusion of the pupil and iris bombé were not observed during the hypertensive phase produced in rabbits' eyes by Diisopropyl Fluorophosphate (DFP) and nitrogen mustard, iridectomies did diminish their glaucomatous effect. The beneficial effect of the operations did not depend on the correction of mechanical factors. It suggested to the authors that the effect of iridectomies in the human may not depend

exclusively on the relief of iris bombé.

Dr. Benjamin J. Wolpaw reported on the incidence of undiagnosed glaucoma in the adult population.

Dr. E. Howard Bedrossian gave a very interesting report of his tonographic observations in some unusual types of glaucoma.

Dr. Edmund B. Spaeth spoke on the evaluation of reoperation for glaucoma. He stressed that reoperative surgery must be based on an accurate analysis of the cause for failure of the former procedure.

Dr. William M. McCarty gave a paper entitled "Latent nystagmus," which covered observations made on over 30 cases including the effect of surgery for any accompanying strabismus, the association of so-called "occlusion hyperphoria," the fusion status, and so forth.

A report on a rare type of bilateral choroiditis with a Kodachrome record for 12 years was read for Dr. Arthur J. Bedell, who was unable personally to attend the meeting.

Dr. Nathan S. Schlezinger and Dr. Robert E. Murto reported on the evaluation of ocular signs and symptoms in 46 patients with proven cerebral aneurysm. Thirty-eight of these cases were of the nonfistulous variety and produced two clinically recognizable syndromes: (1) the ophthalmoplegic syndrome (33 cases), characterized by oculomotor palsies and internal ophthalmoplegia; (2) the prechiasmal and chiasmal syndrome (five cases), which were found to have slow, usually painless loss of visual acuity and diminution in field of vision. Anatomically the ophthalmoplegic syndrome cases were further evaluated from their anatomic location, 28 being supraclinoid and five infraclinoid. The ophthalmoplegic syndrome produced by intracranial aneurysm cannot be localized by ocular signs alone but abnormal pupillary phenomena were present in every case. Infraclinoid aneurysms affected the sixth cranial nerve in a large proportion of the cases, but exact localization on ocular signs is not possible. The present treatment of intracranial aneurysm was discussed.

Dr. James E. Purnell reported on a study of about 100 cases of keratoconus treated with corneal transplantation.

This year's Arthur J. Bedell lecturer, Dr. Algernon B. Reese, was introduced by Dr. Thurber Lewin, president of the Wills Eye Hospital Society. Dr. Reese gave an excellent paper on the diagnosis and treatment of orbital tumors and simulating lesions. About 15 important tumors of the orbit were presented as important from the standpoint of diagnosis. The similarity between tumors of the lacrimal gland and tumors of the parotid gland was described. Dr. Reese emphasized that in removing tumors of the lacrimal gland, not only the entire capsule should be included but the tissue adjacent to the capsule in order to avoid recurrence. He accompanied his lecture with a splendid movie showing a modification of the Krönlein approach for orbital and lacrimal gland tumors.

An outstanding color television program was presented again this year by members of the staff, through the courtesy of their across-the-street neighbors, Smith, Kline & French Laboratories.

The increasing importance and popularity of the Wills Eye Hospital Annual Conferences was evidenced in the fact that 30 exhibitors displayed their wares at this year's meeting and Coca-Cola was freely dispensed for the first time.

The gracious surroundings of the Philadelphia Union League Club made the Friday evening informal reception and supper for both doctors and wives a most enjoyable occasion.

The Wills Eye Hospital Society held its annual business meeting and dinner at the Union League Club on Saturday evening. Elected officers for the coming year are: President, Dr. James H. Delaney, Erie, Pennsylvania; vice-president, Dr. Warren Reese, Philadelphia; and secretary-treasurer, Dr. Roscoe J. Kennedy, Cleveland, Ohio.

Kenneth L. Roper

## OBITUARIES

GEORGE H. CROSS  
(1881-1954)

Although George H. Cross had not been in active practice since 1948, his death on November 23, 1954, at Rehoboth Beach, Delaware, was unexpected. George H. Cross, the son of Dr. George Daniel Cross and Rhoda Esther Howard Cross, was born in Merced, California, on November 1, 1881. He received his preliminary education at the Central Manual Training School in Philadelphia. He entered Jefferson Medical College but transferred after his freshman year to the University of Pennsylvania, from which he was graduated in 1908. His father was an ophthalmologist and also an optician, and the younger Cross spent many hours of apprenticeship working in the Cross Jewelry and Optical Company in Chester, Pennsylvania.



GEORGE H. CROSS

Dr. George H. Cross practiced ophthalmology in Chester, Pennsylvania, and much of his creative ability in the design and construction of instruments and equipment may be attributed to the training and experience gained in the optical shop in his early days. He was best known for his studies on the removal of intraocular foreign bodies and developed a biplane fluoroscope for the removal of nonmagnetic foreign bodies.

He was appointed ophthalmologist to the Chester Hospital in 1913. During his long career he was on the staff of the Wills Eye Hospital and the Beebe Hospital in Lewes, Delaware. He was an assistant professor of ophthalmology in the Graduate School of Medicine of the University of Pennsylvania. Dr. Cross served in the Medical Corps of the United States Army in World War I with the rank of captain.

In 1921 he served as president of the Delaware County Medical Society and held numerous other offices in local societies. He was a member of the American Ophthalmological Society and the Academy of Ophthalmology and Otolaryngology.

Dr. Cross married Caroline May Righter in Ridley Park, Pennsylvania, on December 26, 1906. She predeceased him in 1947. He remarried in 1953 and his wife, three sons, and one daughter survive him.

Dr. Cross enjoyed a large and active practice and had the respect of his colleagues. It is with deep regret that we record the passing of an accomplished associate.

P. Robb McDonald.

STEPHEN L. POLYAK  
(1889-1955)

Stephen L. Polyak, physician, neurologist, anatomist, and investigator died in his sleep March 9, 1955, at the age of 64 years. His monograph, "The retina," exhaustively described the anatomy and histology of this structure and may well remain the standard morphologic reference for decades. A companion study, similarly comprehensive, "The



STEPHEN L. POLYAK

vertebrate visual system," will be published early in 1956 and was completed despite a chronic heart ailment and failing vision that had incapacitated him for years.

Polyak was born in Croatia (now part of Yugoslavia) in 1889 and received the Doctor of Medicine degree from the University of Zagreb in 1920. He taught neurology there until 1928 when he came to the University of California as assistant professor of neuro-anatomy. In 1930 he came to the University of Chicago as assistant professor of neurology and Douglas Smith research fellow. He subsequently transferred to the Anatomy Department and served as professor from 1942 until his death.

His interest in the eye was initiated by the successful application of Golgi's method to the demonstration of individual synapses of neurons in the retina. His scholarship and curiosity were such that he could not then rest content until he had studied the minute anatomy of the retina, its central connections, and then the history of the investigation of vision, optics, and the anatomy and histology of the visual system. By sheer in-

tensity of purpose he pushed to completion his final study while so ill he could work but a fraction some days while on many others he was entirely incapacitated. He is survived by his wife and son.

Frank W. Newell.

## CORRESPONDENCE

REQUEST FOR NONMAGNETIC FOREIGN BODIES  
Editor,  
American Journal of Ophthalmology:

In connection with further development of an electromagnet\* for removing nonmagnetic metal objects from the eye I would like as much information as possible on the composition and size of such objects. In particular, it is desirable to learn what proportion of the accidents encountered in civilian practice involve particles as large as one mm. in smallest dimension, and how many cases occur annually in a geographic district, and what is the distribution as to lead, brass, copper, and aluminum.

If possible I would like to obtain actual objects recovered from lost eyes for examination and for testing with the electromagnet. In some instances these can be reimplanted in animal eyes.

For some time this undertaking was supported by the Office of the Surgeon General of the Army. A paper<sup>†</sup> was submitted by a team at the XVII International Congress of Ophthalmology, September, 1954, and a motion picture made by the Ocular Research Unit of Walter Reed Army Hospital was presented showing copper and aluminum objects one to two mm. in size being extracted from animal eyes, and a two-mm. piece of brass being drawn through vitreous. Since the motion picture was made, the pull has been doubled and effort is being directed

\* Lovell, W. V.: An electromagnet for nonmagnetic substances. *Physical Rev.*, March, 1946, p. 251.

† King, J. H., Jr., Lovell, W. V., Den, A. A. J., Stow, N. N., and Hughes, W. C.: The extraction of intraocular, nonferrous metallic foreign bodies: Preliminary experiments with a new electronic magnet.



toward further increases of attractive force, especially on smaller objects.

Though not an ophthalmologist, I am deeply interested in seeing this undertaking carried to a successful conclusion and the co-operation of your readers in giving information and specimen objects will be greatly appreciated.

(Signed) W. V. Lovell, E.E.,  
Lovell Research Laboratory  
Route one, Box 243  
Sanford, Florida

#### BETA RADIATION THERAPY

Editor,  
American Journal of Ophthalmology

In the March issue of THE AMERICAN JOURNAL OF OPHTHALMOLOGY under "Society Proceedings," following the paper "Beta radiation therapy" by Dr. William F. Hughes, Jr., my discussion was printed. Unfortunately this discussion was apparently submitted as an uncorrected stenographic report for there are approximately 30 errors which make it unreadable and even meaningless in some portions. By the omission of some words, by the inclusion of phrases at the end of one sentence instead of at the beginning of the next, and by substitution for words of similar sounding ones with totally different meanings, the content of some paragraphs has been radically changed. The percent of surface dose reaching the lens at varying distance in millimeters, for instance, was quoted as "millimeters of radium element reaching the lens." The final blow was when I quoted from Krohmer. His statistics were not only garbled, but his name was actually spelled "Clem."

I wish to disclaim responsibility for this discussion as printed and I also suggest that when discussions are lengthy and of a technical nature, the recording secretaries would do well to submit a manuscript to the discussor for official correction before publication. I realize, of course, that in this case the

mistake was primarily that of the society recorder.

Since both the wording and meaning of this discussion is extremely faulty, I hope you will publish my disclaimer. If space permits, it might be appropriate to reprint the discussion as actually delivered. I am enclosing the correct version which I think will still be of general interest.

(Signed) Brendan D. Leahey,  
Lowell, Massachusetts.

#### CORRECTED DISCUSSION

DR. BRENDAN LEAHEY: We have been using a beta applicator here and in the office for a little over five years now; and at the present time have over 300 cases with probably a total of 1,800 treatments. These are all with a radium D applicator. Originally, we had a 10 mc. applicator. Finally we changed it, almost five years ago, to a 22 mc. one. We have not treated any deep lesions; that is, no tumors, nor malignancies of any sort. We have been primarily interested in eye work and corneal vascular lesions or other superficial eye lesions.

It is obvious to any of you that if there are two methods to do the same job, the safest one is the one we would usually choose. Apparently, of the cases we have seen, about 90 percent do respond to radium D. This is more expensive than the strontium (about five or six times the expense); but it is definitely nonpenetrating. Beyond two mm. there is only one percent of the surface dose. At three mm., where you may begin to hit the equator of the lens with a shallow chamber, there is practically no residual radiation; whereas with the radon or strontium 90, you still have somewhere around eight to 11 percent, depending on how it is measured. That isn't very much if you have just one area, but you must remember that the area of the applicator is about five mm. in diameter—5.6—and if you have a completely vascularized cornea, it takes about four treatment areas to cover the whole thing. If you have, as I say, eight percent reaching the lens from

one area you will have, if you treat four different areas, a total equivalent to 32 percent of one treatment reaching the lens.

Besides the two cataracts that Dr. Hughes has reported, down at Hopkins last year, a doctor from New Orleans reported three cases in the New Orleans area from the strontium 90. I don't think these have made the literature yet.

It seems to me that if the strontium 90 applicators do number 330 at the present time, we are going to have a great epidemic of cataracts in the next few years if markedly vascularized cases are treated with strontium.

Radon is by far the most efficient applicator; the radium D, radium, or strontium cannot compare with the radon applicator in this respect. Dr. Hughes has modestly held back, but his radon applicator is certainly the most effective of any and has a wider safety margin in regard to gamma and total body radiation that might affect the patient or operator than other radium element or radon applicators. I would much rather be behind his radon applicator than any of the other radium element or radon ones for any prolonged length of time.

It is impossible to have an all-purpose applicator, the same as it is impossible to have one type of X-ray radiation that will do all jobs and take care of all tumors; so I think the ideal thing would probably be to use radium D for superficial lesions comprising the great majority, and use strontium 90, radium, or radon for the few deep ones.

The ordinary ophthalmologist is not going to treat tumors, and won't even treat epitheliomas. They will go to the roentgenologist who knows more about that type of lesion. We have been interested here primarily in the corneal pathologic conditions and we also see a great many vernal catarrh cases. I think in the vernal cases, radium D, while it works pretty well, is not as effective.

\* \* \*

I might answer in response to the question just asked that this radiation is not a cure for

vernal conjunctivitis except temporarily; but there is no reason why these patients couldn't come back one or two years later if necessary. If follicles are more than 1.5 or 2.0 mm. in size, to get a good result, it is necessary to shave these off first above the level of the conjunctiva. When you shave these off, you can start beta right away and get a very nice result.

In general, from the standpoint of the margin of safety, if you will confine yourself to more superficial lesions, you will be much better off with radium D. The cornea, of course, is only about 0.8 of a mm. thick, and we have had no trouble in removing almost complete corneal vascularization even almost at the back of the cornea. The main problem we have had is the chemical burns that Dr. Hughes spoke of. We have had very little luck just radiating chemical burns—sulfur dioxide, lime burns, or other burns. The proper treatment of these is complete resection of the surrounding conjunctiva taking care of all the large trunks; then we go ahead with beta radiation starting three days later; and we have made those eyes completely avascular in quite a number of cases.

\* \* \*

DR. HUGHES (referring to the New Orleans radiation cataracts): I think it was a radium applicator because they haven't used strontium yet as far as I know.

DR. LEAHEY: The radium applicator has a smaller percentage of surface dose reaching the lens than strontium has—only about 50 percent of the strontium amount—that would make it even more favorable. I believe at three mm. less radiation from radium element reaches the lens than from either radon or strontium, less of surface dose, I mean.

DR. HUGHES: I don't believe it is so, that less radiation, percentagewise, from the radium applicator reaches the lens than with radon.

DR. LEAHEY: Krohmer's figures at three mm. were something like 3.9 percent of surface dose for radium or about one third what it was for radon or strontium 90, but at five

mm., percentage of surface dose was about the same. Two, three, and four mm. are also less with radium element; a smaller percentage of surface dose reaches those depths.

(Dr. Hughes completed the discussion as originally printed.)

## BOOK REVIEWS

**VIRAL AND RICKETTSIAL DISEASES OF THE SKIN, EYE, AND MUCOUS MEMBRANES OF MAN.** Harvey Blank and Geoffrey Rake. Boston and Toronto, Little, Brown & Co., 1955. 285 pages, 36 color and 65 black and white illustrations. Price: \$8.50.

Many excellent volumes on general virology have appeared in the past several years but few have made any attempt to cover adequately the viral and rickettsial infections that involve the skin, the eye, and the mucous membranes. In the present volume the many important diseases affecting these structures are described clearly, concisely, and thoroughly, and with abundantly illustrative diagrams, photographs, and drawings, many of them in color. As would be expected, the diseases to the knowledge of which the authors themselves have made important contributions, such as herpes simplex and lymphogranuloma venereum, are covered most fully and authoritatively. The chapter on herpes simplex, for example, contains a great deal of new information not to be found in other texts and will make highly profitable reading for every ophthalmologist. The host-parasite relationship between man and virus, as expressed in dendritic keratitis is especially well delineated.

Other viral diseases affecting the eye that are discussed include trachoma, inclusion conjunctivitis, molluscum contagiosum, herpes zoster, vaccinia and variola, Newcastle disease, lymphogranuloma venereum, measles, warts, epidemic keratoconjunctivitis, and superficial punctate keratitis. It is unfortunate that the recent studies conducted by Huebner and his associates at the Na-

tional Microbiological Institute on epidemic follicular conjunctivitis due to Type-3 strains of the adenoido-pharyngeal-conjunctival (APC) viruses were reported too late to be included. In addition to the sections on individual diseases, there are two introductory chapters dealing with the nature of viruses and rickettsiae, and with the diagnosis of viral and rickettsial infections.

The final chapter deals with the 11 rickettsial infections of importance to man. These diseases are of only minor interest to the ophthalmologist, however, since scrub typhus is the only rickettsial disease in which important eye changes occur. These changes include retinal hemorrhages and exudates. Only minor conjunctival inflammations are seen in the other rickettsial infections.

Phillips Thygeson.

**CURRENT THERAPY 1955.** Edited by Howard F. Conn, M.D. Philadelphia, W. B. Saunders Company, 1955. 651 pages, index. Price: \$11.00.

It is amazing to note that among the several hundred contributors to this annual edition of a book giving the "latest approved methods of treatment for the practicing physician," there is not to be found the name of a single ophthalmologist. Every other specialty in medicine appears to be represented, but apparently the practicing physician is not presumed to encounter such conditions as glaucoma, iritis, or conjunctivitis. The only reference to conjunctivitis in the index is in relation to beryllium poisoning, certainly a rare disorder to be encountered by the general practitioner.

One minor improvement is noted. In the 1954 edition local cortisone was recommended for the treatment of herpes simplex of the cornea, but the current edition noted that this is not without danger and recommends that an ophthalmologist should be consulted (certainly excellent advice).

It is of course questionable as to how much ophthalmic therapy should be included. In a

book of this scope, however, it would appear that at least some reference should be made to the more commonly encountered ocular conditions. One has to search carefully to find an occasional casual reference to the eye made by the neurologist, allergist, or dermatologist.

William A. Mann.

**HUMAN PHYSIOLOGY.** By B. A. Houssay, M.D., J. T. Lewis, M.D., O. Orias, M.D., E. Braun-Menéndez, M.D., E. Hug, M.D., V. G. Foglia, M.D., and L. F. Leloir, M.D. Translated into English by J. T. Lewis, M.D., and O. T. Lewis. New York, McGraw-Hill Book Co., 1955. Second Edition. 1,177 pages, 504 figures, bibliography, and index. Price: \$12.00.

The present edition of this outstanding contribution contains 59 more pages, and five more figures than the first edition reviewed in *THE JOURNAL* (34:1767, December, 1951). There is also a notable absence of typographical errors, yet the price is \$2.00 less. The Argentine authors, for years exclusively engaged in teaching and research, have achieved so successfully a balanced account of the whole field of human physiology that repeated editions of their fine work are now available in Spanish, Portuguese, French, and English. The treatment of endocrine physiology contributed by Houssay, the Nobel Prize winner in 1947 for his work on the hormones of the pituitary gland, is, as anticipated, of outstanding excellence. The remarkable popularity of this textbook is dramatic testimony to the universality of modern medical science.

The succinct comprehensive account of ocular physiology in 46 pages is ideal for undergraduate study and well exemplifies the characteristic "wise discrimination between the little that can be taught and the far wider field that must be left out." It is nevertheless up-to-date with bibliography as late as 1952 and refers to the recent work on rhodopsin, color vision, hyaluronidase, cataract produc-

tion by tryptophane-free diets, and the cytochrome-oxidase system in the crystalline lens. Additional material throughout the text illustrates the guiding thesis that "the whole organism is an indivisible anatomic and functional unit."

James E. Lebensohn.

**HYDROSTATICS AND HYDRODYNAMICS OF THE EYE.** By Wiktor Arkin. Bucharest, State office of medical publications, 1953. 391 pages, no figures, no index. Price: Not listed.

The author presents a considerable volume of information concerning the movements of fluids in the eye. Known facts about permeability of tissue membranes for different substances are described, including factors which influence the rate of passage of these substances.

Formation of aqueous is divided in two phases: one is secretion of water by all tissues in the eye; the other is the secretion of electrolytes by the ciliary body, controlling the intraocular osmotic pressure. The forces acting in the movement of the aqueous from the eye are: the hydrostatic differential on both sides of the blood aqueous barrier and the difference in the osmotic pressures. The aqueous flows out mainly through the angle of the anterior chamber. There is some outflow of fluid through the choroid, the retina, and the optic nerve.

In the chapter dealing with the intraocular pressure the author describes the method of elastometry of Kalfa, which is related to balistography, and the measurement of corneal elasticity by Friedenwald.

All the factors influencing the level of pressure are discussed in detail. The author does not consider blocking of the angle of the anterior chamber by the iris to be the main cause of congestive glaucoma. He feels that the slowing down of outflow of fluid is located in the area of the angle, in the efferent duct connecting Schlemm's canal and the aqueous veins. The influence of congestion of



the choroid and the ciliary body is stressed and the changes in the reaction of small blood vessels are noticed.

Chapters on hypotony of the eye, on causes and distribution of ocular hemorrhages, and on edema of different ocular tissues complete the monograph. Eleven pages of bibliography are the proof of the thoroughness with which it was written.

Sylvan Brandon.

---

HUNDREDTH YEAR CELEBRATION OF THE BIRTH OF PAUL EHRLICH AND EMIL V. BEHRING. Frankfurt am Main, Farbwerke-Hoechst, 1954. 39 pages, 42 photographs. Price: Not listed.

From March 14 to 16, 1954, the medical world paid its profound respects to Ehrlich and v. Behring in honor of the hundredth anniversary of their births. The festival was held in Frankfurt, with music, opera, speeches, and feasts. This booklet commemorates the occasion and consists of excellent candid photographs of the many worldwide-known medical celebrities who were there. The volume closes with a touching letter from Albert Schweitzer. To those who were privileged to attend the celebration, this book is a priceless souvenir; to the rest, it is full of interest and should become a medical collector's item of rarity.

Derrick Vail.

---

HYPEROSTOSIS CRANII. By Sherwood Moore, M.D. Springfield, Illinois, Charles C Thomas, 1955. 226 pages, 107 illustrations, bibliography. Price: \$10.50.

Hyperostosis cranii was adequately described by G. Morgagni in 1765. It has gained clinical recognition as a syndrome largely because of the investigations of J. Stewart (1928) and F. Morel (1930). Sherwood Moore, whose name is closely associated with this syndrome, began to collect material 25 years ago. Because of the scarcity of cases, the existing filed material was scru-

tinized. Though Moore is a roentgenologist, he considers not only the roentgenologic aspects but also aspects of symptomatology and differential diagnosis, etiology, pathology, and treatment. He even includes a chapter on paleopathology.

For those ophthalmologists who may not be familiar with Morgagni's syndrome, a brief description of this anomaly follows. The disease occurs predominantly in women. The outstanding characteristics are obesity, hirsutism, and hyperostosis of the skull. Less frequent symptoms are headaches, muscular weakness, and an apathetic facial expression. Mental disorders often accompany these symptoms.

Though this picture is occasionally referred to as "hyperostosis frontalis interna," Moore was able to recognize three additional forms, namely nebula frontalis, hyperostosis fronto-occipitalis, and hyperostosis calvariae diffusa. All these are varying stages of the same process. The extent of the roentgenologic findings seems to be unrelated to the severity of the clinical picture. Bilaterality distinguishes the process from inflammatory or neoplastic involvement of the skull.

The etiology of the disease is unknown. Treatment is purely symptomatic. Two cases reported by M. Falconer and B. Pierard in 1950 may be of interest to the ophthalmologist. They found that bony spicules in the optic canal caused damage to the optic nerve which was successfully treated by decompression. In 14 percent of his series, Moore found "visual disorders" which, however, were so varied that they could not be catalogued satisfactorily.

It is impossible for me to evaluate the importance of Morgagni's syndrome in general or this book's contribution to the existing literature. However, it appears to be quite obvious that acquaintance with it will not materially aid the ophthalmologist in his field.

Stefan Van Wien.



NEURO-OPHTHALMOLOGY. By Donald J. Lyle. Springfield, Illinois, Charles C Thomas, 1954. Second edition. 591 pages, 335 figures, references, index. Price: \$17.50.

The author, professor and director of the Department of Ophthalmology, College of Medicine, University of Cincinnati, is well known in the field of ophthalmology and particularly for his work in the first edition of this book.

It is gratifying to all of us to know that there is a strong demand for work of this kind. The first edition had a second printing in 1947. The present edition is greatly enlarged, containing more than 140 new figures and 15 new charts. The printing is a masterpiece of clarity of the text and illustrations and neither the author nor the publisher has cut corners. The result is a splendid book for reading and reference.

In the preface, Dr. Lyle quotes Harvey Cushing "They (the ophthalmologist and neuro-surgeon), however, have much to learn from one another and between them an answer should be forthcoming to the moot questions." However, it will be recalled that it was the influence of Cushing that has caused a number of his students and followers to ignore the ophthalmologist in the work-up of many of their cases, particularly regarding reports on the optic papilla and the careful fields of vision studies. In fact, in some places the neuro-surgeon either takes his own fields or delegates this important phase of neurologic study to his resident or even to the senior medical student.

The cause of this separation may well be the fault of ophthalmology. For, in the past, few ophthalmologists have been particularly

interested in the neurologic aspect of our field and even the newer crop of residents has been reluctant to devote much time and attention to the subject of neuro-ophthalmology. This is not good. The subject is a most important one and can be a fascinating and rewarding study.

The present work is especially valuable in the exposition of the basic knowledge that is required for an understanding of this involved subject. The parts of the chapters devoted to this phase are particularly good and beautifully illustrated. One of the finest chapters is that on the arteriovascular and arteriovenous systems of brain and eye. Another equally valuable chapter is that on the syndromes which include eye symptoms.

We are grateful to Dr. Lyle for the splendid job he has done for ophthalmology.

Derrick Vail.

#### BOOKS RECEIVED FOR REVIEW

*The following books have been received for review. Acknowledgment is made here because often there is a delay before a suitable review appears.*

TRANSACTIONS OF THE AMERICAN OPHTHALMOLOGICAL SOCIETY 1954. Volume LII. New York, Columbia University Press, 1955. Price: Not listed.

A SWIMMING PROGRAM FOR BLIND CHILDREN. By Robert Belenky. American Foundation for the Blind, 15 West 16th Street, New York 11, New York. Price: \$0.45.

1955 MEDICAL PROGRESS. Edited by Morris Fishbein, M.D. New York, The Blakiston Division, McGraw-Hill Book Company, Inc., 1955. Price: \$5.00.

A STUDY OF THE LIVING EXPENSES OF BLIND PERSONS. By Nathaniel J. Raskin. American Foundation for the Blind, 15 West 16th Street, New York 11, New York. Price \$0.50.

FOURTH ANNUAL REPORT ON STRESS. By Hans Selye, M.D., and Gunnar Heuser, M.D. Montreal, Canada, Acta, Inc., 1955. Price: Not listed.

## ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

### CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

### 3

#### VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

D'Esposito, Mario. **Metabolism of the retina and choroid following the use of placental extract.** *Rassegna ital. d'ottal.* 23:397-411, Sept.-Oct., 1954.

After briefly reviewing the literature concerning the use of Filatow's placental extract, the author presents the results obtained in in-vitro studies with Warburg's manometric method. He discusses the influence of Lioplacantyl (Maestretti) on the metabolism of the retina and choroid. From rather extensive studies he concludes that there is a moderate effect of the preparation on the oxygen consumption of the retina, a very moderate influence on the anaerobic glycolysis and no effect on the oxygen consumption in the choroid. (6 tables, 18 references)

Eugene M. Blake.

Fornaro, L., and Lepri, G. **Comparison of the action of ACTH, cortisone and hydrocortisone upon the evolution of experimental retinitis pigmentosa.** *Rassegna ital. d'ottal.* 23:366-374, Sept.-Oct., 1954.

The writers studied experimentally the therapeutic action of ACTH, cortisone

and hydrocortisone in the retinitis produced in rabbits by the use of sodium iodide. The action of cortisone and hydrocortisone was similar to that of ACTH but was limited to the period of treatment, whereas that of ACTH resulted in a sustained action for some time after suspension of treatment. This suggests that the action of ACTH is more than the well-known effect of stimulating the suprarenal glands but also a direct effect on the retina. It remains, therefore, to ascertain whether some other factor or principle, for example the melanophores, may be involved. (3 figures, 13 references)

Eugene M. Blake.

Gemolotto, Guglielmo. **Electrophoretic studies on the lens of rabbits with retinal degeneration following section of the optic nerve.** *Ann. di ottal.* 80:333-337, 1954.

The electrophoretic pattern in the lens of five rabbits with retinal degeneration after optic nerve section showed an increase of alpha-proteins and a decrease of beta-proteins. These variations are similar to those reported in retinal degeneration from chemical substances and are a result of the degenerative process of the retina. (15 references) John J. Stern.

Iida, M. **Phosphatase of cornea.** Acta Soc. Ophth. Japan 59:44-58, and 109-122, Jan. and Feb., 1955.

Iida describes the advantages and disadvantages of various histochemical procedures in the demonstration of phosphatase in the cornea and the influence of fixatives and the optimum pH for staining. It takes only half an hour to stain phosphatases in the epithelium but 12 hours to stain them in the endothelium. In the developing chick embryo, phosphatases in the cornea increase after the thirteenth day of incubation. By dipping the corneal section in insulin and cortisone, a considerable decrease in acid phosphatase reaction is brought about. After injury of the cornea, the alkaline phosphatase decreases considerably during the first six hours, but it increases again after 24 to 48 hours. In stored cornea the alkaline phosphatase in the endothelium decreases during the first three hours, but it increases again after the sixth hour. (17 figures, 6 tables, 104 references) Yukihiro Mitsui.

Ikeda, I., Komi, T., Minami, M., Miyazawa, M., Nakaji, H., Sakamoto, Y., Yanagida, H., Nishiwaki, Y., and Murata S. **The influence of oscillation and electroshock on the blood-aqueous barrier.** Acta Soc. Ophth. Japan 59:162-164, Feb., 1955.

The authors point out the disadvantages of fluorescein determination in the aqueous by fluorescence. They use radioactive sodium di-iodo-fluorescein as a tracer to be measured with the Geiger counter. They refer to the published fact that the transit of fluorescein into the anterior chamber is increased by oscillation and electroshock. They consider, however, that this is not due to an increased permeability of the blood-aqueous barrier. They found that by oscillation and shock an increase in fluorescein concentration occurred in the blood stream. No

increase in the ratio of fluorescein concentration in the aqueous over that in the blood followed oscillation. They conclude that oscillation and shock cause a fluorescein mobilization into the blood but do not cause an increased permeability of the blood-aqueous barrier. (1 table, 5 references) Yukihiro Mitsui.

Nakayama, Y. **Side effects of antibiotics by subconjunctival injection.** Acta Soc. Ophth. Japan, 59:148-162, Feb., 1955.

A subconjunctival injection of most antibiotics in a concentration of 10 mg./ml. and 1 mg./ml. is irritating. The clinical changes in rabbits are hyperemia, swelling and cloudiness of the conjunctiva with secretion. Polymorphonuclear leucocytes are predominant in the discharge. By biopsy an infiltration of polymorphonuclear cells with a small number of lymphocytes is observed. These histologic changes disappear within two days in most cases. A similar change is brought about by an injection of varidase. (16 figures, 4 tables, 14 references) Yukihiro Mitsui.

Nordman, J., Mandel, P., and Achard, M. **Inhibition of sugar metabolism in the lens.** Brit. J. Ophth. 38:673-679, Nov., 1954.

The eyes of calves were used in these experiments in which the sugar metabolism of the lenses was blocked in vitro. Actual differences in opacity are easily measured by placing the two lenses on a grid and photographing them. One of the two lenses of a pair of eyes was placed in a solution comparable to aqueous humor and the other in a solution containing an inhibitor to sugar metabolism. The inhibitors used were monoiodoacetic acid, sodium fluoride, phoridzine, sodium malonate and fluoroacetic acid. The lenses remained submerged in the solutions for periods varying from 6 hours to 10 days. The results indicated that interference

with sugar metabolism is always followed by some cataractous changes. Although each of these substances inhibits metabolism in a different manner, each one caused marked opacification of the lens. (1 figure, 7 tables, 10 references)

Morris Kaplan.

della Porta, Vittorio. **The serum-protein pattern in the so-called thrombosis of the retinal vein.** *Ann. di ottal.* 80:319-332, 1954.

The serum-protein pattern was studied in 12 patients with retinal venous thrombosis. The studies consisted of estimations of the total protein level, electrophoretic analysis, analysis of the euglobulin fractions and nine reactions of colloidal sero-lability. There was a constant low albumin level, occasional increase of alpha- and beta-globulin, regular increase of gamma-globulin. The sero-colloidal reactions were all positive. The sero-protein pattern therefore reveals a productive "mesenchymopathy." (9 references)

John J. Stern.

de Vincentiis, Mario. **Nitrogen concentration of the vitreous in experimental degeneration of the retina.** *Rassegna ital. d'ottal.* 23:393-396, Sept.-Oct., 1954.

The author studied the nitrogen concentration in the vitreous in experimental degeneration of the retina, which resulted from the use of either monoacetic iodide of sodium, from resection of the optic nerve, or from the chorioretinitis following cyclodiathermy. An increase in the protein nitrogen content was demonstrated, more especially with the retinitis following the use of monoacetic iodide. The results obtained substantiate the hypothesis of the precocious electrophoretic modification of the lens. In conditions with abnormal accumulation of vitreous protein the protein arises for the most part from the retina. This may account for the secondary alterations of lens

substance in such conditions. (2 tables, 8 references)

Eugene M. Blake.

Watillon, M., Prijot, E., and Weekers, R. **Experimental modifications of the resistance to the outflow of the aqueous.** *Bull. Soc. belge d'opht.* 107:374-383, June, 1954.

This splendid work consists of two parts. In the first part changes in the resistance of the aqueous outflow were caused by anatomic conditions, either by damage to the trabeculum or by occlusion of the chamber angle. In the second part the resistance to the outflow of the aqueous was reduced by the use of hyaluronidase and the response of a trabeculum deprived of hyaluronic acid was investigated. Barany's procedures were followed in animal eyes. The eyes were enucleated 15 to 20 minutes after death and perfused 30 to 50 minutes. No refrigeration was used. These experiments proved that physical, chemical and enzymatic factors influence the resistance to the outflow of aqueous. Compression of the trabeculum by increase of the perfusion-pressure and partial occlusion of the chamber angle increase the resistance to the outflow. Hyaluronidase, probably by depolymerization of hyaluronic acid in the trabeculum decreases the resistance to the outflow. (2 graphs, 1 table, 2 references)

Alice R. Deutsch.

#### 4

#### PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Bellouard, F. **Monocular diplopia with coexisting normal and abnormal retinal correspondences.** *Arch. oftal.* Buenos Aires 29:383-393, July, 1954.

Monocular diplopia, or binocular tripplopia, is occasionally met with in cases of strabismus submitted to orthoptic training. The condition is usually due to the awakening of normal retinal correspondence before the old, abnormal sen-



serial relationship has completely faded away. According to the author's views it could be elicited only when binocular stimulation takes place. Two cases of this phenomenon are presented, which occurred in children, 6 and 10 years of age. (7 figures, 10 references)

A. Urrets-Zavalía, Jr.

McGraw, J. L., and Enoch, J. M. **Contact lenses—an evaluating study.** *Tr. Am. Acad. Ophth.* 58:561-574, July-Aug., 1954.

The authors discuss the various contact lenses and their relation to the development of halo, corneal turbidity or haze, and to visual acuity, photophobia, dark adaptation, muscle balance, entoptic field changes, color vision, depth perception, visual fields and clinical appearance of the conjunctiva and cornea. Special studies were made of subjects wearing contact lenses in a hot room, a cold room, and a low pressure chamber. The fields and protective factors of contact lenses were also studied. The authors also discuss the advantage and disadvantages of contact lenses. (12 figures, 1 table, 8 references)

Theodore M. Shapira.

Morgan, Meredith W., Jr. **A unique case of double monocular diplopia.** *Am. J. Optometry* 32:70-87, 1955.

This is an extraordinary case report of a young woman with what appeared to be diplopia and anomalous retinal correspondence symmetrical in both eyes. The tests devised for study of the case included refraction, motility, pin hole, stenopaic slit, ophthalmometer, orthoptic, ophthalmoscopic, Maxwell's spot, color fusion, stereopsis, measurement of Panum's areas, diplopia fields and tachistoscopic tests, etc.

Paul W. Miles.

Sato, Tutomu. **The surgical treatment of astigmatism.** *Klin. Monatsbl. f. Augenh.* 126:16-31, 1955.

Seven methods for the surgical correction of various grades and kinds of astigmatism are described. The operations consist of a number of corneal incisions, perforating or non-perforating, made with an especially delicate knife. Incisions from the posterior surface are more effective than those from the anterior surface. The direction of the incision depends on the axis of the astigmatism. Four of these procedures are designed to correct myopic astigmatism. A mixed astigmatism can be corrected by the interlamellar preparation and sliding of corneal flaps. (40 figures, 22 references)

Frederick C. Blodi.

Schober, Herbert. **Glasses impervious to ultraviolet against asthenopia.** *Klin. Monatsbl. f. Augenh.* 126:81-82, 1955.

In fluorescent light the ultraviolet rays cause a fluorescence of the crystalline lens which may lie like a veil over the entire field. If glasses are worn that absorb these rays the visual acuity may increase and asthenopia may disappear. (4 references)

Frederick C. Blodi.

## 5

### DIAGNOSIS AND THERAPY

Dejean, C., and Jaulmes, M. **Recent progress in anesthesia in ophthalmology.** *Arch. d'opht.* 14:679-690, 1954.

The authors note the great progress made recently in anesthesia and discuss the application of this progress to eye surgery. They note the necessity for ophthalmologists to understand the mechanism of action of the recently introduced adjuvants to local anesthesia in order to employ them properly. They discuss in some detail the problem of postoperative vomiting and report progress in its control. They mention particularly the value of nautamine and bromanautine as antiemetics and also urge the use of  $\frac{1}{4}$  mg. atropine intravenously as an emergency measure in nauseated patients. Other



antiemetic agents that they have tried include largactil, which also has a hypnotic action, and nembutal. They note that the effects of curare can be toxic and variable and state their belief that the drug should be used only in complicated operations in tense patients with increased intraocular pressure. The various preoperative and postoperative medications and the various anesthesia techniques are discussed in detail.

P. Thygeson.

Kiehn, Clifford L. **Mucous membrane grafts.** *Am. J. Surg.* 87:715-721, May, 1954.

In deformities of the fornix the inferior sulcus is often obliterated so that a prosthetic eye cannot be retained. The author uses mucous membrane grafts and prepares the recipient sulcus by making an incision just lateral and inferior to the outer canthus of the eye in a normal skin fold. By sharp dissection a tunnel is formed from the incision to the inner canthus above the infraorbital ridge and just under the conjunctiva or scar tissue. Dental compound is then softened and inserted in the tunnel and allowed to harden. It is then removed and dried thoroughly. A full thickness mucous membrane graft is removed from the buccal surface of the mouth. An area 6 by 8 cm. has been removed by the author for orbital and other mucosal repairs, and in all cases the buccal surface has healed promptly without fibrosis or cicatricial contracture. In the removal of the mucosa Stenson's duct is carefully avoided.

Dermatome glue is placed on the stent and allowed to become sticky. The graft is wrapped and sutured about the stent and inserted in the tunnel. The skin and subcutaneous tissues are closed in the usual manner. After 14 days an incision is made through the conjunctiva directly over the tunnel intraorbitally. The scar is excised and the edges of the mucous

membrane graft and the conjunctiva are sutured together. A conformer is then inserted to keep the graft distended. The excess tissue in the distal ends of the tunnel is excised. The skin incisions are then closed. The prosthetic eye can be securely placed in this sulcus.

Excellent explanatory drawings and illustrative photographs accompany the article, showing the use of this technique in specific cases. Alston Callahan.

Rouher, P., and Cantat, A. **Hypnotic medication before, during, and after operation in ocular surgery of the adult.** *Arch. d'ophth.* 14:698-706, 1954.

The authors describe in detail their experiences with hypnotics in 250 cases in which they had no serious accidents. Their technique consists in the administration by mouth the night before surgery of phenergan and eunocet, and of largactil intramuscularly. In the morning two hours before surgery they give nembutal by suppository, and  $\frac{1}{4}$  of an hour before surgery a mixture intramuscularly of dolosal, phenergan, and largactil. Their dosages and technique are varied according to the age of the patient and his state of health. The period of hypnosis generally lasts from 10 to 15 hours. The authors state that the advantages of their method include a suppression of all anxiety, immobilization of the patient and his eye, and hypotony of the globe.

P. Thygeson.

Yamada, K. **The relation between retinal blood pressure and cerebrospinal fluid pressure.** *Acta Soc. Ophth. Japan* 59:91-95, and 99-108, Jan., 1955.

In normal man the diastolic pressure of the retinal artery and the spinal fluid pressure have a relationship and the correlation coefficient is 0.453. The ratio between the latter and the systolic pressure is small and the coefficient is 0.392. Neither the systolic nor the diastolic pres-

sure of the systemic artery has a close correlation with the spinal pressure. In patients with essential hypertension the situation is quite the same. This fact indicates that an increase in arterial pressure of the fundus and that of the system are not parallel, whereas the former and an increase in the spinal pressure are proportionate. (6 figures, 16 tables, 37 references)

Yukihiko Mitsui.

## 6

### OCULAR MOTILITY

Allen, Merrill J. **A simple photographic method for continuously recording vertical and horizontal eye movements.** *Am. J. Optometry*. 32:88, 93, 1955.

The ophthalmograph was adapted to record horizontal eye movements in one eye and vertical in the other continuously during various industrial tasks. The method should prove useful in eye movement research.

Paul W. Miles.

Daenen, P., and Weekers, R. **Indications for myotomy of the inferior oblique muscle in concomitant esotropia.** *Bull. soc. Belge d'opht.* 107:357-365, June, 1954.

Concomitant convergent strabismus often is accompanied by an overaction of one or both inferior oblique muscles. If unilateral, the vertical deviation chiefly affects the deviating eye in adduction. If bilateral, the overaction may be more pronounced in the nonfixating eye or may be equally marked in both eyes. The pathogenesis of this abnormality is obscure. The authors do not believe that the initial disturbance could be a congenital paralysis of the superior oblique muscle because they saw overactive inferior oblique muscles in late accommodative types of squint without any paralysis or in cases of high anisometropia, namely in patients lacking binocular functions entirely. The final achievement in the

surgical treatment of those patients depends on the characteristics of the individual case and is either cosmetic and functional or only cosmetic. The treatment of choice is the transconjunctival myotomy of one or both inferior oblique muscles or their bulbar insertion. In very severe cases a myectomy up to 3 mm., combined with the indicated surgery on the horizontally acting rectus muscles is suggested. Pre- and postsurgical photographs prove the effectiveness of the surgical procedures. (7 figures)

Alice R. Deutsch.

Gordon, Orville E. **A study of primary and auxiliary medial ocular rotation.** *Tr. Am. Acad. Ophth.* 58:553-560, July-Aug., 1954.

The author points out that the lateral and medial rectus muscles of the eye lie in contact with the eyeball for a distance between the anatomic insertion and the effective physiologic insertion; this is called the arc of contact. When the eye is turned in the direction of the muscle, the muscle will unwrap as the anatomic insertion approaches the physiologic. Though this fact is stated in textbooks, no record of measurements or analysis of the importance of this action in ocular movement have been recorded. The author made such measurement on twelve anatomic specimens and six surgical patients. His analysis of the data is not only interesting but practically important. He shows that a component of the total function of the superior and inferior rectus muscles is necessary for the accomplishment of further external rotation after the eye has been rotated enough to unwrap the arc of contact of the lateral rectus muscle. (2 figures, 6 tables, 5 references)

Theodore M. Shapira.

Hiroishi, M., and Kawaoka, H. **Studies of the electro-oculogram. VI Dynamic analyses of eye movement and its clinical**

**application.** *Acta Soc. Ophth. Japan* 59: 169-174, Feb., 1955.

A dynamic analysis of ocular movements by means of the E.O.G. and an artificial eye model showed the velocity of horizontal ocular movement to be about 10 rad./sec., and its force about 500 dynes. The H-h-curve (H for height of position record, h for height of velocity record) is very important in the analysis of muscular action by means of the E.O.G. Standard H-h-curves are shown in the figures. If there are complicated disturbances in more than two muscles, the analysis of E.O.G. is sometimes difficult. However, when the H-h-curve is employed in such a case, the affected muscle and even the degree of the affection can clearly be analysed. (5 figures, 1 table, 4 references) Yukihiro Mitsui.

de Jaeger, A., and Berdolet, J. **Surgery of non-concomitant strabismus.** *Bull. Soc. belge d'opht.* 107:349-357, June, 1954.

A patient with paralytic squint should not be operated on as long as an improvement in the motility of the paralyzed muscle can be expected, usually not before six months. The surgery should never be postponed when muscle rigidity of the homolateral antagonist or heterolateral synergist occurs because structural or degenerative changes in those muscles would permanently impair a restoration of complete function. The diagnostic procedures, their interpretation in presurgical examinations and the methods and amounts of surgery in paralytic squints are reviewed and evaluated. (1 figure, 8 references) A. R. Deutsch.

Law, Frank W. **Squint operations and binocular function.** *Tr. Am. Acad. Ophth.* 58:546-552, July-Aug., 1954.

For this review, the author has taken from his private practice a series of 40 consecutive unselected cases of concomitant strabismus in which surgery had been

done. He brings out the following points. In a child whose deviation starts at birth, it is a rare exception to obtain a binocular result. After surgery and orthoptics, it is unusual for a patient to have better binocular vision than that with which he started. Well established abnormal retinal correspondence is now incurable. A proportion of patients fail to respond to occlusion, even under eight years of age; there are other occult reasons for amblyopia than disuse. Alternation merely is an incidental hazard and does not materially affect the binocular prognosis. Suppression (without amblyopia) is not considered a hopeless bar to achieving binocular single vision. If binocular single vision is likely, the sooner surgery is done, the better. If not, cosmetic operation is desirable and delay is pointless. In successful strabismus surgery, the permanency of result depends upon the binocular state of the patient. Orthoptic treatment is useless, considered from the aspect of eliminating an angle between the visual axes. It can in most cases only exercise, exploit, and facilitate the initial binocular state; it cannot improve it. The immense value of orthoptics in the diagnosis and the treatment of heterophorias is not in question. (5 references)

Theodore M. Shapira.

Norbis, A. L., and Malbrán, E. **Paralysis of the inferior oblique muscle.** *Arch. oftal. Buenos Aires* 29:413-423, July, 1954.

Among 320 patients with disturbances of motility who were examined in the course of six months, five cases of unilateral inferior oblique palsy were found. In two of them the condition made its appearance in adult life and was clearly acquired, whereas in the remaining three, in which it had been present from early childhood, it may have been congenital. Operative correction, with at least good cosmetic results, was performed by means

of one or several of the following procedures, used either alone or in association with some surgery of the medial or lateral rectus muscles: advancement and myectomy of the affected muscle, controlled tenotomy of the contracted, homolateral superior oblique and moderate recession of the hyperactive, contralateral superior rectus. (8 figures, 15 references)

A. Urrets-Zavalía, Jr.

## 7

### CONJUNCTIVA, CORNEA, SCLERA

Agarwal, L. P., and Adhauia, H. N. **Role of Vitamin A in the healing of corneal ulcers.** *Ophthalmologica* 128:6-14, July, 1954.

Supplementary vitamin A was administered intramuscularly to half of 60 patients with corneal ulcers who received identical topical antibiotic treatment and showed no signs of vitamin A deficiency. The authors' observations suggest that the vitamin A medication was beneficial in that it shortened the healing time and reduced the density of the final scar. (9 tables, 22 references)

Peter C. Kronfeld.

Agarwal, L. P., and Saxena, R. P. **Erythromycin in trachoma.** *Brit. J. Ophth.* 38:690-691, Nov., 1954.

In this study of 100 patients who had trachoma with inclusion bodies, 50 served as controls and were given no treatment whatever, and 50 received erythromycin orally and by instillation of ointment two or three times daily. The untreated patients showed no change after six weeks whereas those who were given treatment started responding within 24 hours. Subjective symptoms disappeared within three days. There was retrogression of pannus in half of the patients and the inclusion bodies disappeared in all of them. Drug reactions were rare. (1 table, 2 references)

Morris Kaplan.

Chinaglia, Vincenzo. **Dermatitis of Duhring-Brocq and pemphigoid affections of the ocular mucous membranes.** *Ann. di ottal.* 80:291-318, 1954.

The literature is reviewed and one case in a 67-year-old woman is described in detail. She had bilateral pemphigus of the eyes during a relapse of a bullous dermatitis diagnosed as herpetiform dermatitis of Duhring-Brocq. Similar lesions were present in the oral and pharyngeal mucous membranes. In the right eye the final result was symblepharon, blepharophimosis, keratosis of conjunctiva and cornea, and xerosis. The left eye recovered almost entirely under therapy with aureomycin, sulfanilamide, penicillin and vitamins. A biopsy showed subacute inflammation and keratinization of the epithelium. The differential diagnosis between pemphigus and Duhring-Brocq dermatitis is discussed. The hypothesis of a virus infection is accepted but it is admitted that clinical, morphologic, histopathologic and bacteriologic elements fail to allow a differentiation between the two conditions. (6 figures, 80 references)

John J. Stern.

Halbertsma, K. T. A. **Epithelioma of the tarsal conjunctiva.** *Ophthalmologica* 128:1-6, July, 1954.

A fairly well circumscribed, slowly growing tumor of the palpebral conjunctiva in a 68-year-old woman was excised and found to be a squamous cell carcinoma. A recurrence responded well to X-ray therapy. The literature concerning this fairly rare, but typical tumor is reviewed. (4 figures, 12 references)

Peter C. Kronfeld.

Lagos, E. J. J. **Marginal dystrophy of the cornea (Terrien's disease). Report of a case.** *Arch. oftal. Buenos Aires* 29:365-372, July, 1954.

Consisting mainly of an extensive, peripheral, furrow-shaped atrophy of the



corneal parenchyma, which may lead to the development of large amounts of irregular astigmatism and to severe visual impairment, this rare degenerative condition usually stands forth in young adults and may end after a period of years by the formation of a subepithelial prolapse of the iris and even by rupture of the eyeball.

The case of a 45-year-old woman is presented, whose eyes were both affected and who would have experienced considerable improvement after some topical applications of trichloroacetic acid. (2 figures)  
A. Urrets-Zavalía, Jr.

de Leonibus, F., and Gemolotto, G. **Microanatomic study of a case of blue sclera.** *Boll. d'ocul.* 33:789-795, Dec., 1954.

One eye of a four-year-old girl had to be enucleated after a perforating injury. The sister of her mother had otosclerosis and blue scleras; the father of the patient had high myopia and retinal detachment. The specimen showed a corneal thickness of 0.3 mm., the sclera measured 0.4 mm. Dissociation of the connective tissue and formation of lacunae, and an unusual quantity of free mucopolysaccharids found in the sclera after staining with toluidine blue, Rinehart's and Abul-Haj's stain, indicate a break-down of scleral collagenous substances as the possible explanation of the syndrome of blue sclera. (5 figures, 8 references)  
K. W. Ascher.

Pavkovic-Bugarli, G., and Cvetojevic, M. **Terramycin in trachoma.** *Brit. J. Ophth.* 38:692-698, Nov., 1954.

In the province of Vojvodina, Jugoslavia, trachoma is very common but there are very few acute cases. A chronic follicular form of the disease with very little severe pannus or lid damage occurs with great frequency. Eighty patients were treated; all were given terramycin locally and some were given sulphonamides orally in addition. The terramycin was

applied in an ointment six times daily. There was very little change during the first two months of treatment, but during the third month improvement was quite marked. Vision was considerably improved in all cases and the drug unmistakably benefited patients with true pannus. Of the 80 patients 37 were clinically cured (4 of 7 patients in stage I, 24 of 40 in stage II, and 9 of 33 in stage III). When combined with sulfathiazole, terramycin produced quicker and better results than when used alone. (6 figures, 22 references)  
Morris Kaplan.

Popp, Klaus. **Corneal erosions with polyethylenglycols.** *Klin. Monatsbl. f. Augenh.* 126:76-77, 1955.

Ophthalmic ointments now produced without polyethylenglycol have proved to be of great value in the treatment of corneal erosions. Polyethylenglycol alone was irritating to the conjunctiva and damaged the cornea of experimental animals.  
Frederick C. Blodi.

## 8

### UVEA, SYMPATHETIC DISEASE, AQUEOUS

François, J., and Beheydt, J. **Bilateral heterochromia of Fuchs.** *Bull. Soc. belge d'opht.* 107:365-373, June, 1954.

Among about 40 cases of heterochromia of Fuchs four patients with bilateral lesions were observed. The bilateral disease is not easy to diagnose as the difference in color in the two irides is not as conspicuous as in monocular lesions. Attention is called to certain diagnostic peculiarities. If both eyes are affected, the disease starts more or less simultaneously in both eyes but the course is often different, and the cataract may occur in one eye much sooner than in the other. Other characteristics are the fine corneal precipitates, the absence of posterior synechias, the iris atrophy and the absence of any inflammatory reaction. Gonioscopic examination



shows no abnormality except for the presence of vascular loops at the root of the iris. Puncture of the anterior chamber shows an absence of inflammatory cells, an increase of albumen content to 0.5 to 1.0 percent, and filiform hemorrhage, mostly opposite the place of puncture. The pupil does not dilate normally after instillation of 1-percent benzedrine. The cataract extraction is usually easy but the prognosis is impaired because of the frequency of postoperative glaucoma (33 percent in the bilateral cases). (14 references)

Alice R. Deutsch.

Schoepfer, Otto. **Postiritic, pigmented pseudotumors of the chamber angle.** *Klin. Monatsbl. f. Augenh.* 126:73-75, 1955.

The authors observed three patients in whom a pigmented tumor developed in the chamber angle. This occurred after an iritis and the cystic character of this pseudotumor could be suspected. The most important diagnostic sign differentiating the lesion from a true melanoma was a depigmentation of a segment of the iris which developed soon after the cyst had formed. (6 figures, 1 reference)

Frederick C. Blodi.

## 9

### GLAUCOMA AND OCULAR TENSION

Alearts, M. L. **The atrophies of the temporal iris-quadrant in chronic glaucoma.** *Bull. Soc. belge d'opht.* 107:219-223, June, 1954.

Progressive, essential atrophy of the iris, occurring in association with, or preceding glaucoma always starts in the temporal superior quadrant and advances toward the inferior nasal quadrant. The decolorization extends from the pupillary margin to the root of the iris, the normal iris pattern and the marking of the collarette disappear, showing a wasting of the mesodermal layers, including the sphincter, and simulating a thickening of the pupillary margin. An increased dens-

ity of the vessel walls with partial or complete obstruction of the lumen and degeneration of the nerve fibers were found in pathologic specimens. A vascular origin of the glaucomatous atrophy is reasonably certain; no explanation could be found for its characteristic starting point, its counterclockwise progression in the right eye and clockwise progression in the left or its complete absence, with normal iris structure, in many cases of glaucoma. Among the author's 224 cases of glaucoma, 197 eyes which had been operated upon had a more or less complete sectorshaped iris atrophy; among the 27 not operated upon 24 eyes had the sectorshaped iris atrophy. (12 references)

Alice R. Deutsch.

ten Doesschate, J., and Lansberg, M. **P. Glaucoma and the function of the labyrinth.** *Bull. Soc. belge d'opht.* 107:205-207, June, 1954.

A relationship between glaucoma, Ménière's symptom-complex and hypacusia has been mentioned several times in ophthalmic publications. With this in view, 26 unselected glaucoma patients were checked by audiometer tests and the findings were tabulated. It was found that hypacusia occurred frequently simultaneously with chronic glaucoma. Hypacusia occurred especially in women with chronic glaucoma and high tension, not to be controlled with miotics. The association hypacusia with high tension seemed to be more significant than hypacusia with field loss. (1 table)

Alice R. Deutsch.

Gildemyn, M. H. **Iridencleisis in secondary glaucoma following cataract extraction.** *Bull. de la Soc. belge d'opht.* 107:268-275, June, 1954.

An iridencleisis from below was successfully performed in two patients who had secondary glaucoma following minor injuries to eyes, and who had been re-

cently operated upon for cataract. The postoperative course was uneventful, no synechias between the anterior hyaloid membrane and the surgical wound occurred, the tension stayed normal and the vision was very satisfactory. (2 figures, 19 references) Alice R. Deutsch.

Kleinert, Heinz. **The aqueous outflow after cyclodialysis.** *Ophthalmologica* 128: 44-53, July, 1954.

For the study of aqueous outflow the author has used a new method which consists of the injection into the anterior chamber, by means of Amsler's cannula, of a measured amount of .1 percent sodium fluorescein in normal saline. Rate and route of elimination of this fluid are determined by repeated tonometry and biomicroscopic observation of the epibulbar vessels (cfr. *Klin. Monatsbl. f. Augenh.* 122:665, 1953). Application of this method to three cyclodialyzed human eyes shows that such eyes are capable of eliminating the injected fluid rapidly through channels other than the epibulbar vessels. This elimination, the author believes, does not take place through the cyclodialysis cleft into the choroidal veins, but rather through other channels with low resistance, possibly through the corneoscleral trabeculae, the canal of Schlemm and its posterior vascular connections. Although he has not made any fluorometric measurement of the disappearance rate of fluorescein from the anterior chamber, the author considers Goldman's concept of a reduction in aqueous flow after cyclodialysis very unlikely. In his experience the persistence of a supraciliary cleft is not essential for the proper functioning of a cyclodialysis. (1 figure, 6 references) Peter C. Kronfeld.

Kleinert, Heinz. **The posterior sclerectomy.** *Klin. Monatsbl. f. Augenh.* 126: 31-41, 1955.

This operation was devised by Lindner

as an emergency procedure in cases of high intraocular pressure which could not be influenced by medical means; 288 such operations are reported as a final summary because modern medical treatment makes this operation superfluous. A definite surgical procedure against glaucoma should follow within ten days. In six percent of the eyes retinal detachment or severe retinal or vitreous hemorrhages with permanent impairment of vision occurred. (9 references)

Frederick C. Blodi.

Marchi, F. **Rapid changes in the depth of the anterior chamber of a glaucomatous eye with subluxated lens.** *Boll. d'ocul.* 33: 842-845, Dec., 1954.

A 75-year-old man with subluxated lens and glaucoma of long standing showed a normal anterior chamber when looking upward, and an apparently 6 mm.-deep anterior chamber when looking down. No vitreous hernia seemed to be present. There were no synechiae present; discontinuation of the use of miotics interfered with the phenomenon. The possible mechanism of these changes is discussed. K. W. Ascher.

Weekers, R., Prijot, E., Delmarcelle, Y., and Gustin, J. **Physiologic and pathologic determinant causes in the control of intraocular hypertension in chronic simple glaucoma.** *Bull. Soc. belge d'opht.* 107:208-219, June, 1954.

Early diagnosis of chronic simple glaucoma is of considerable social importance. Frequent tonography and frequent tonometry in persons 50 years old or more are recommended and standardization of tonometers as done by the U.S.A. committee on standardization is suggested. The ocular tension in 300 normal subjects was checked and tabulated. A tension higher than 25 mm. Hg. was considered to be pathologic and a tension of 24 was called suspicious. The effect of pilocarpin,

eserine, D.F.P. and mintacol on the resistance to the outflow of aqueous is discussed. The advantages of a 0.01-percent D.F.P. solution is explained. The extended effect of a 2-percent adrenaline solution on the production of aqueous is interpreted and the benefits of its use as well as its hazards in possible congestive glaucoma are reviewed. In the follow-up studies frequent checks of central visual fields with small targets are necessary, especially in patients not under complete control. Iridencleisis is the surgery of choice, followed by retrociliary nonperforating diathermy if the tension should not be controlled. D.F.P. should not be used before surgery because it disposes to posterior synechias. The ophthalmologic examination of members of the family of glaucoma patients would help early detection of this disease. (4 tables)

Alice R. Deutsch.

## 10

### CRYSTALLINE LENS

Kirby, D. B., Atkinson, W. S., Davis, F. A., Fry, W. E., Vail, D., McLean, J. M., Clark, W. B., Chandler, P. A., and Guyton, J. S. **Symposium: Cataract extraction.** Tr. Am. Acad. Ophth. 58:327-419, May-June, 1954.

Kirby, D. B. Introduction. pp. 325-326. As moderator of this extensive discussion Kirby made some preliminary remarks. He pointed out that the time for surgery arrives when the patient's vision is no longer adequate for his use. He emphasized his belief that each surgeon should be ready to change procedures according to indications as the operation progresses, should observe the effect of each manipulation and then apply the next step as indicated.

Atkinson, W. S. Preparation of patient. pp. 327-333. The author discusses pre-anesthetic preparation, sedation and analgesia, and anesthesia (topical, akinesia

and retrobulbar). He states that cataract surgery is safe and easy if attention is given to these procedures in relation to the individual patient. (3 figures, 9 references)

Davis, F. A. Incision and closure, iridotomy and iridectomy, principles of wound healing. pp. 334-360. Davis describes the various methods for iridectomy, iridotomy, and the incision and closure of the wound. He discusses the principles of wound healing and describes the post-operative management of the patient. (13 figures, 16 references)

Fry, W. E. Extracapsular extraction. pp. 361-366. The author describes the planned and the unplanned techniques of of extracapsular cataract extractions. (6 figures)

Vail, D. Intracapsular extraction: Mechanics, technique, variations. pp. 367-370. Vail reviews the development and structure of the vitreous and the zonule and their relation to the lens capsule in order to make clear the importance of an understanding of each detail of procedure in the removal of the lens in its capsule.

McLean, J. M. Extraction in complicated cases. pp. 371-377. The author discusses planned variations and modifications of technique used in pre-existing or anticipated complications which may arise in any of the usual steps of the operation. (10 figures)

Clark, W. B. Complications occurring during surgery. pp. 378-381. The complications discussed by the author are: toxicity of drugs used for hypnosis and analgesia, retrobulbar hemorrhage, formation of hematoma, inadequate exposure, complications due to errors of technique, oozing from small conjunctival blood vessels, hemorrhage, constriction of the pupil, complications of intracapsular extraction and loss of vitreous.

Chandler, P. A. Complications after cataract extraction: clinical aspects. pp. 382-396. The author discusses the causes,

consequences, and treatment of the various complications: flat anterior chamber; prolapse of iris; incarceration of iris in the wound; incarceration of lens capsule in wound; hemorrhage into anterior chamber or vitreous or both; expulsive hemorrhage; rupture of the wound; iritis and uveitis; corneal edema; pupillary membrane; drawn-up pupil; atrophy of the globe; epithelization of the anterior chamber; macular degeneration; glaucoma and detachment of the retina. He briefly mentions infections. (1 figure, 23 references)

Guyton, J. S. Complications after cataract extraction: Pathologic aspects. pp. 397-407. The pathologic aspects of the complications are clarified by the discussion of histologic preparations which are presented in the illustrations. (30 figures)

Kirby, D. B. Summary. pp. 407-412. After some general remarks which underline the importance of fundamentals on which the essayists are in agreement, Kirby describes in detail some ideas and procedures which have been uniformly successful in his own practice.

Discussion. pp. 413-419. After Kirby's summary the members of the panel answered specific questions which had been asked by some of the listeners.

Theodore M. Shapira.

Marretta, Pier Vittorio. **Intravenous anesthesia in cataract extraction.** *Rassegna ital. d'ottal.* 23:412-416, Sept.-Oct., 1954.

No unfavorable effects have been observed, either early or late, from the use of pentothal sodium given intravenously before cataract operations. A certain amount of hypotony occurs but without ill effect. The use of the barbiturate is especially desirable with highly nervous and hypertensive patients. (17 references)

Eugene M. Blake.

Velhagen, K. **The principle of puncture in a discission.** *Klin. Monatsbl. f. Augenh.* 126:8-16, 1955.

Some of the complications and dangers of a discission are first discussed. Infections and hemorrhages are rare nowadays. A retinal detachment may follow, but is often unavoidable and is another reason to prefer an intracapsular extraction. Corneal opacities and glaucoma may occur.

In order to obtain a satisfactory hole in the membrane, a pre-operative slitlamp examination is most important. The pupil should be of normal width and not in mydriasis. The knife should be actually on the membrane before the incision is started. The author uses a double-edged, angled knife or a double-edged Graefe knife. (4 figures) Frederick C. Blodi.

Wiedersheim, O., and Kessler, W. **Experiences with cataract extractions.** *Klin. Monatsbl. f. Augenh.* 126:1-8, 1955.

This is a statistical report on more than 500 extractions. The authors use a fornix-based flap and only conjunctival sutures. Less than 50 percent of the operations were truly intracapsular. Unusual is the method of repairing an iris prolapse. A small prolapse is only cauterized, but a larger prolapse is excised after eight days to avoid severe vitreous loss. (3 figures, 4 charts, 17 references)

Frederick C. Blodi.

## 11

### RETINA AND VITREOUS

Appelmanns, M., and Lamotte, R. **Blood coagulation in thrombosis of the retinal vein.** *Bull. Soc. belge d'opht.* 107:300-323, June, 1954.

The purpose of this study is an evaluation of the controversial anticoagulant therapy in thrombosis of the retinal vein. Three hematologic tests, namely pro-



thrombin time, recalcification, and tolerance of the plasma towards heparin were performed in fifteen patients with thrombosis of the retinal vein. It was realized that it is extremely difficult to prove an increase in blood coagulation, especially as factors might be present in the body which are not demonstrable in vitro. Abnormalities of the coagulation were not considered to be the fundamental cause of thrombosis of the central vein, none the less anticoagulants were suggested as treatment of choice because the obstruction might not have been complete and it was possible that complete blocking might be prevented and collateral circulation promoted by anticoagulant medication. Anticoagulants can limit the size of the thrombus and, due to a thrombolytic action, can promote recanalization of the vein. The drugs suggested for treatment were heparin and dicumerol and its derivatives. Considerable attention was paid to the exact dosage and to the simultaneous use of vasodilating drugs because of their prevention of a slowing of the bloodstream. Clinical, histopathologic and historic data on central vein thrombosis are reviewed in the introductory chapters. (3 figures, 4 tables, 24 references)

Alice R. Deutsch.

Brihaye, Van Geertruyden, Danis, P., and Zylberszac. **Fundus changes in disseminated lupus erythematosus. (Second anatomical-clinical observation).** Bull. Soc. belge d'opht. 107:284-296, June, 1954.

Regular fundus examinations were made in a 47-year-old woman who had atypical lupus erythematosus. She had the characteristic changes in lymph nodes, muscles, joints and lungs and characteristic cells were found in the blood smear, but she had no skin or heart lesions. The cotton-wool patches in the retina showed a certain cyclic development, first a loose, fluffy patch, getting larger and denser,

then, after a stage of stabilization, the outline became blurred and the lesions vanished without a trace. In spite of this cycle a definite relationship between an increase of retinal exudation and an impairment of the general health could be seen. The exudate in the retina proved to be cytooid bodies when seen in histologic preparations. There was also a decrease in ganglion cells, an increase in neuroglia, a thickening of the intima of the choroidal and retinal vessels and a mild infiltration of the choroid. Similar fundus observations verified by pathologic examinations were made previously in a case of typical lupus erythematosus. However the fundus changes are not diagnostic for they were also seen in scleroderma, polyarteritis nodosa and dermomyositis. (4 figures, 28 references)

Alice R. Deutsch.

Dieterle, P. **The importance of electroretinography in the differential diagnosis between primary and secondary tapetoretinal degeneration.** Arch. d'opht. 14:707-716, 1954.

The author reports two cases which indicate that in primary retinitis pigmentosa the b wave of the ERG is completely absent. When a peripheral crescent of visual field is active, the a wave can be present. In secondary tapetoretinal degeneration both waves are present. The prognostic value of the ERG is considered. Finally Dieterle notes that with the ERG it is possible to show objectively that retinitis pigmentosa may occur after measles.

P. Thygeson.

François, J., and de Rank, A. **Retinography in myopia and retinal detachment.** Bull. Soc. belge d'opht. 107:323-349, June, 1954.

The changes in the electroretinogram (ERG) in 10 cases of simple myopia and in 60 cases of malignant myopia and 35



cases of retinal detachment were investigated. The ERG was registered on Elmquist's electrocardiograph, modified by Karpe. The ERG was normal in every case of simple myopia. In the malignant progressive type of myopia the amplitude of the b wave was subnormal (less than 0.25 mv) in about 75 percent of the cases and was independent of the degree of choroidal degeneration. It was often found to have become abnormal at a time when no fundus changes were visible and remained unchanged in spite of continuous impairment of the choroidal structures. It disappeared entirely when the stage of total choroidal atrophy was reached. No correlation between the amplitude of the b wave and the degree of myopia could be established. The ERG in retinal detachment is either subnormal or absent. It depends not only on the extent and duration of the detachment but also on the vital qualities of the retina. The b wave is more pronounced after successful detachment operation than before operation. It remains decreased in monochromatic blue light. The ERG is unessential in evaluation of a pre-operative prognosis because the operation may be successful after a negative preoperative response. (26 figures, 1 table, 9 references)

Alice R. Deutsch.

Sengupta, M. **Neovascularization of the disc in chronic simple glaucoma.** *Brit. J. Ophthalm.* 38:684-689, Nov., 1954.

Four patients, over 50 years of age, who developed new veins in the disc in the course of chronic simple glaucoma are described. These new-formed loops between the central vein and a large branch probably resulted from pressure of the artery on the branch, made worse by both the glaucoma and some sclerosis of the artery. Through the new vessel the venous return is carried on unhampered. (3 figures, 7 references) Morris Kaplan.

Zanen, M., and Lempereur. **Another case of vitelliform cyst in the macular region.** *Bull. Soc. belge d'opht.* 107:296-300, June, 1954.

The record of an eight-year-old boy with peculiar macular lesions and surprisingly good vision are discussed. The fundus of the left eye showed a yellowish sharply delimited and mildly elevated round lesion as large as the optic disc. The lesion in the right eye was  $\frac{1}{2}$  d.d. in diameter and showed a red mottling on a yellow background. This lesion was considered to be a more advanced stage of the same disease. The pathogenesis, differential diagnosis and other similar case histories are briefly reviewed. (2 figures, 1 table, 5 references)

Alice R. Deutsch.

### 13

#### NEURO-OPHTHALMOLOGY

Cavka, Vladimir. **Ophthalmoneurologic symptoms resulting from prefrontal leucotomies.** *Ophthalmologica* 128:15-22, July, 1954.

For the treatment of schizophrenia the author performs transorbital, prefrontal leucotomies. The present communication concerns itself with the ophthalmoneurologic symptoms resulting from the lobotomy which are anisokoria in every case, conjugate deviation in about half of the cases, exotropia in a third of the cases and, rarely, monocular nystagmus. (7 references) Peter C. Kronfeld.

François, J., and Neetens, A. **The Foster-Kennedy (F.K.) syndrome.** *Bull. Soc. belge d'opht.* 107:402-443, June, 1954.

The Foster-Kennedy syndrome consists of monocular optic atrophy, ipsilateral anosmia and contralateral papilledema which may lead to secondary optic atrophy. Two patients with this syndrome were observed by the authors. One patient

had opticochiasmatic arachnoiditis and sclerosis of the internal carotid artery. The other had a malignant myxochondroma of the ethmoids which invaded the oral cavity and the base of the skull with destruction of the sella and encroachment of the sphenoidal fissure. After reviewing a long series of published cases the authors emphasize the characteristic clinical significance of the syndrome but minimize the diagnostic value or etiological importance attributed to it in the past. The syndrome may occur without a tumor; if a tumor is present it might be located anywhere in the cranial cavity. The combination of the syndrome with a bilateral inferior quadrantic hemianopsia in a person over 50 years of age is suggestive of opticochiasmatic arachnoiditis with or without vascular changes, and not of an intracranial tumor. The unilateral anosmia should not be evaluated as a specific sign before nasal disease has been considered. Many variations of the syndrome have been described. They represent different stages of an intracranial disease, of which the syndrome itself only coincides with a specific period. The rate of the progression of the inflammatory, vascular or neoplastic disease, the direction of progression, and the age and general health of the patient influence the ophthalmologic picture and the preservation of vision. (8 figures, 1 table, 106 references)

Alice R. Deutsch.

François, J., and Verriest, G. **Campimetry in reduced illumination in neuroophthalmology.** Bull. Soc. belge d'opht. 107:224-267, June, 1954.

The photopic and scotopic functions of the visual apparatus in relation to neuroophthalmologic abnormalities are reviewed. The addition of field and campimetric studies in reduced illumination to the routine perimetry increases the diagnostic value of these procedures consider-

ably. Scotopic campimetry is more sensitive to central defects than photopic campimetry. Peripheral defects in the isopters are better revealed in an illuminated field but their specific individual characteristics show up more distinctly in the dark; because of the absence of the physiologic slopes in the scotopic fields the relative borders of the defects correspond better to the extent of the lesions, whereas the defects in the peripheral photopic fields are exaggerated, in comparison with the anatomic lesion. The opposite is true for the central field. In the lighted field the defects correspond to the anatomic damage and are difficult to detect when they are small, but might be more easily uncovered in reduced illumination. Routine perimetry, testing of the adaptation threshold, and adaptation determination of the curve should always precede the taking of the scotopic fields. The examiner should be familiar with the variations of the S.S.O. (scotome central à l'obscur) and with the different techniques in all those procedures. He also should have the necessary patience to undertake these detailed investigations.

Thirty-five case histories include the records of patients with papillitis, retrobulbar neuritis, primary and secondary optic atrophy, lesions of the chiasm and optic tract and diseases of the optic radiation. The results of these findings demonstrate the practical importance of the described technique with which minute central field defects can be disclosed which could not have been uncovered by any other method. (10 figures, 69 references)

Alice R. Deutsch.

Kanter, Detlev. **The jaw-winking phenomenon.** Klin. Monatsbl. f. Augenh. 126: 50-59, 1955.

The author describes eight cases of this phenomenon which he saw in his practice during the last two years. In one patient

the condition was bilateral. Supranuclear changes are assumed to be the cause for this aberrant innervation. The treatment is not discussed. (12 figures, 2 tables, 23 references) Frederick C. Blodi.

Matteucci, P., and Kluzer, G. **Foveal vision in homonymous hemianopsia.** *Rassegna ital. d'ottal.* 23:357-365, Sept-Oct., 1954.

The authors studied 30 cases of homonymous hemianopsia in subjects with temporal, parietal and occipital tumors and also in some with temporal and occipital lobectomy and focal epilepsy. Field studies were made with the perimeters of Maggiore and of Goldman, and central campimetry was done with the Bjerrum screen and the Landolt-Amsler test. Three cases are described and the fields and diagrams showing the location of lesions are shown. The authors feel that their observations confirm the existence of "macula sparing" in homonymous hemianopsia and that the great problem is one of campimetric technique. In all 30 cases examined there was macular sparing and when the lesion was behind the geniculate bodies macular vision was good, which is attributed to preservation of the cones. The experience in cases of occipital lobectomy confirms the belief in double representation of the macula. (6 figures, 12 references) Eugene M. Blake.

Oshima, Y. **Fatigability of central field in subclinical beriberi amblyopia.** *Acta Soc. Opth.* Japan 59:22-28, and 143-148, Jan.-Feb., 1955.

In a subclinical amblyopia due to vitamin B<sub>1</sub> deficiency, vision seems normal but a central scotoma which is labile in form and extension is demonstrable and this is due to a fatigability of the central field. The patients complain of asthenopia. (7 tables, 23 references)

Yukihiko Mitsui.

Páez Allende, F. **Bilateral palsy of the orbicularis oculi muscle. Report of a case.** *Arch. oftal.* Buenos Aires 29:395-400, July, 1954.

The case of a 47-year-old man is presented, in whom a bilateral, complete inability to close the palpebral slits arose suddenly, in association with some motor loss in the right arm and leg. The extrinsic ocular musculature was normal, as were also the fundus, the media, the fields and the visual acuity. On the other hand, Argyll Robertson pupils were present. The condition, which remained unchanged for 12 months, was attributed to syphilis. (2 figures, 3 references)

A. Urrets-Zavalía, Jr.

## 14

### EYEBALL, ORBIT, SINUSES

Alport, B., and Dame, L. R. **Orbital cholesteatoma: report of a case.** *Tr. Am. Acad. Opth.* 58:575-579, July-Aug., 1954.

A differential diagnosis of orbital tumor is presented with history, clinical findings and complete recovery. Sections were presented to pathologists and diagnosis concurred in. (4 figures, 3 references)

Theodore M. Shapira.

Schmedes, Rudolf. **Orbital complications of retained teeth.** *Klin. Monatsbl. f. Augenh.* 126:77-79, 1955.

A 43-year-old woman had exophthalmus on the left side for one year and hyperopia in that eye. X-ray examination revealed a cloudy left antrum with two retained teeth in it. The antrum was cleaned and the teeth extracted. (4 figures, 3 references)

Frederick C. Blodi.

## 15

### EYELIDS, LACRIMAL APPARATUS

Fox, Sidney A. **Lower lid repair.** *Tr. Am. Acad. Opth.* 58:580-585, July-Aug., 1954.

The author divides these conditions into three groups: those that do not involve the lid margin; those that involve only the anterior half of the lid margin, the ciliary margin; and those that involve the whole margin of the lid. In the first group are lesions such as the xanthomas, fibromas, hemangiomas, and the small epitheliomas. In the other groups are basal cell carcinomas and pigmented tumors. Fox describes the therapeutic procedures used in each group. (9 figures)

Theodore M. Shapira.

Hallermann, W. **Pseudotuberculosis of the lacrimal sac.** *Klin. Monatsbl. f. Augenh.* 126:59-62, 1955.

The extirpated sac showed a granulomatous infection with epithelioid cells and giant cells. In polarized light the giant cells were observed to contain birefractile elements. These were probably talc from a previous operation. (3 figures, 4 references)

Frederick C. Blodi.

Hefel, Ferdinand. **Experiences with the dacryocystorhinostomy of Dupuy-Dutemps.** *Ophthalmologica* 128:61-69, July, 1954.

The Eye Clinic of the University of Graz (Austria) reports 88 percent success of Dupuy-Dutemps' external dacryocystorhinostomy in complete obstruction of the nasolacrimal duct. The operation is well suited for the average ophthalmologist and does not require special experience in tear sac work. (29 references)

Peter C. Kronfeld.

Klemens, F. **A simple procedure to shorten the palpebral fissure.** *Klin. Monatsbl. f. Augenh.* 126:79-80, 1955.

A narrowing of the palpebral fissure by tenotomy of the levator is often unsatisfactory in cases of lagophthalmus after paresis of the facial nerve. The fissure should be shortened by a nasal tar-

sorrhaphy. A small skin flap is mobilized in each lid on the nasal side of the punctum and these flaps sutured together. (2 figures)

Frederick C. Blodi.

Le Grand and Baes. **Unusual papebral granuloma, a case report.** *Bull. de la soc. Belge d'opht.* 107:275-283, June, 1954.

A peculiar granuloma appeared on the upper-lid of a 14-year-old boy several months after having cut this lid in a fall from his bicycle. The primary injury was treated with home remedies. When examined for the first time the growth was adherent to the skin. It was very difficult to excise and a minute nodule remained. From this small nodule another tumor developed in several months. The recurrent tumor was dissected. The boy stayed well after the second operation. The two surgical specimens appeared to be similar. They contained zones of fibrosis, necrotic foci, layers of lymphocytes, epithelioid cells and a few giant cells. The pathologic pattern was practically identical with the one in Boeck's sarcoid. No other lesions could be found in the patient, the sedimentation rate and skin reaction were normal. The hematologic examination disclosed a high eosinophil count. The pattern of the scar, the slow development and benign course and the pathologic picture of the lesion suggested a foreign body reaction, possibly beryllium, though no foreign body could be found in spite of the most careful search. The manifestations of generalized and localized beryllium intoxication are briefly reviewed. (3 figures, 22 references)

Alice R. Deutsch.

Salvi, G. L. **Treatment of the ocular symptoms of Sjögren's disease.** *Boll. d'ocul.* 33:796-806, Dec., 1954.

Salvi used diathermo-coagulation of the lacrimal canaliculi in eight patients who had keratoconjunctivitis sicca for many



years. The occlusion of the canaliculi proved beneficial in all of them while previous treatments, local and general, were not successful. Two patients showed a deterioration when the canaliculi became re-canalized; repetition of diathermic occlusion led to improvement. The author feels that the occlusion of the canaliculi is the only treatment available to bring some relief to sufferers from Sjögren's syndrome. (24 references)

K. W. Ascher.

## 16

### TUMORS

Franceschetti, A., and Babel, J. **Microhemangiomas of the retina.** *Ophthalmologica* 128:23-29, July, 1954.

A slowly growing epi- and juxta-papillary tumor in an otherwise healthy 19-year-old male proved to be a small hemangioma overlaid by marked optic degeneration of the retina (cfr. Reese, Tumors of the Eye, 1951, 350, and Wilder, The Military Surgeon, 99:459, 1946). (5 figures, 7 references)

Peter C. Kronfeld.

Leonhardt, V. A. **Ocular involvement in reticulo-endotheliosis and reticulum cell lymphoma.** *Klin. Monstbl. f. Augenh.* 126:63-72, 1955.

The author observed a 72-year-old woman who suddenly became severely sick. Multiple skin tumors appeared. The

blood picture and the bone marrow revealed a severe anemia and a monocytic leukemia. There were tumors on the lid margins. The fundi showed hemorrhages and cotton-wool patches. At autopsy a reticulum cell lymphoma was found. There were tumor cells in the choroid, the sub-conjunctival tissue and in the orbit. Hemorrhages were found in the retina and in the iris. (8 figures, 19 references)

Frederick C. Blodi.

## 18

### SYSTEMIC DISEASE AND PARASITES

François, J., and Haustrate, L. **Ocular manifestations of Still's disease.** *Bull. Soc. belge d'opht.* 107:383-402, June, 1954.

Iridocyclitis, bandshaped keratitis and cataract in a child represent a clinical entity, pathognomonic for rheumatic disease in this age-group, and referred to as the oculo-articular syndrome. If they appear in a child without joint lesions, fever, enlargement of lymph nodes or splenomegaly the performance of a sedimentation rate and the examination of the anti-streptolysin titer are essential for the confirmation of the diagnosis of infantile rheumatic disease. Early differentiation of the chronic destructive form and Still's peri-articular disease is however not possible. The author reports in detail the case of a two-year-old boy who exhibited this syndrome in both eyes. He also reviews the available literature. (1 figure, 110 references)

Alice R. Deutsch.



## NEWS ITEMS

Edited by Donald J. Lyle, M.D.  
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received at least three months before the date of occurrence.

### DEATH

Dr. Donald Weeks Bogart, New York, New York, died January 28, 1955, aged 49 years.

### ANNOUNCEMENTS

#### TO HONOR DR. BURCHELL

A subscription dinner, honoring Dr. Edgar B. Burchell on the completion of 60 years of distinguished service at the New York Eye and Ear Infirmary, will be given at the Seventh Regiment Mess, 643 Park Avenue at 67th Street, New York, on Friday evening, June 10, 1955. Cocktails and reception will be at 6:30 and dinner at 7:30. For further information write to:

Dr. Joseph H. Krug  
Secretary-Treasurer, Alumni Association  
New York Eye and Ear Infirmary  
Second Avenue and 13th Street  
New York 3, New York

#### ORTHOPTIC EXAMINATIONS

The annual examination of orthoptic technicians by the American Orthoptic Council will be conducted in August and October, 1955. The written examination will be nonassembled and will take place on Thursday, August 25, in certain offices and will be proctored by designated ophthalmologists. The oral and practical examinations will be on Saturday, October 8, in Chicago, just preceding the meeting of the American Academy of Ophthalmology and Otolaryngology.

Applications for examination are now being received by the office of the secretary of the American Orthoptic Council:

Dr. Frank D. Costenbader  
1605 22nd Street, N.W.  
Washington 8, D.C.

Applications, which must be accompanied by the examination fee of \$30.00, will not be accepted after July 1, 1955.

#### CHIBRET GOLD MEDAL 1956

The Chibret Gold Medal, worth 200,000 French francs, will be awarded for the fourth time during the 1956 congress of the Société Française d'Ophtalmologie. The prize may not be divided. The competition is open to trachomatologists of all countries and it may deal with any aspect of trachomatology: clinical, social, preventive, and medical or surgical therapeutics.

The work must be written in French, have a maxi-

mum of 30 typewritten pages, be presented in triplicate, and be accompanied by an abstract of two pages in French and, in so far as possible, in English, Italian, and Spanish.

The jury will include the president of the League against Trachoma, Dr. M. P. Bailliart; the president of the International Organization against Trachoma, Prof. G. B. Bietti; the vice-president, the general secretary, the secretary of the Union française, and the treasurer of the League, together with two members of the board of directors, appointed by drawing.

The prize paper will be published in its entirety in the *Revue Internationale du Trachome*. Abstracts of the other papers submitted will also appear in the *Revue*.

All manuscripts must reach the general secretary of the League:

Dr. Jean Sedan  
94 Rue Silvelle  
Marseille, France

before January 1, 1956.

#### MOTION PICTURE FILMS

The Academy-International of Medicine announces a completely revised fourth edition of "Professional Films" is now in compilation. (The frequency and number of future insert pages necessary to assure a comprehensive index that is continuously current over a period of years will be determined by the volume of forthcoming productions.) It will include new sections providing biographic data on authors, and information on the audiovisual activities of medical schools, dental schools, and graduate teaching centers.

Over 28,000 copies of previous editions are in use by medical and dental schools, program chairman of state and specialty societies, and others here and abroad. AIM provides this valuable audiovisual information to the profession-at-large, without profit, as one of its contributions toward elevating the standards of medical and dental services by expediting the dissemination of professional knowledge.

You are urged to assist directly by (1) informing film authors of this announcement so that they can write for questionnaires, or (2) providing the film title and full name and address of any film author. Write to the Academy-International of Medicine, 601 Louisiana Street, Lawrence, Kansas.

The Scientific Advisory Committee of The National Council to Combat Blindness, Inc., has been

enlarged to 16 members and now includes:

James H. Allen, M.D., chief, Department of Ophthalmology, Tulane University of Louisiana School of Medicine, New Orleans; Alson E. Braley, M.D., director, Department of Ophthalmology, University Hospitals, State University of Iowa College of Medicine, Iowa City; Arthur G. DeVoe, M.D., chief, Department of Ophthalmology, New York University, Bellevue Medical Center, New York; Louis B. Flexner, M.D., professor of anatomy, University of Pennsylvania School of Medicine, Philadelphia; Dan M. Gordon, M.D., assistant professor of clinical surgery, Department of Ophthalmology, New York Hospital-Cornell Medical Center, New York; Charles Haig, Ph.D., professor, Department of Physiology and Pharmacology, New York Medical College, Flower and Fifth Avenue Hospitals, New York; Michael J. Hogan, M.D., professor of ophthalmology, University of California Medical School, San Francisco; Peter C. Kronfeld, M.D., professor of ophthalmology, University of Illinois Medical School, Chicago; A. E. Maumenee, M.D., chief, Division of Ophthalmology, Stanford University School of Medicine, San Francisco; Karl Meyer, M.D., associate professor of biochemistry, College of Physicians and Surgeons, Columbia University, New York; Stuart Mudd, M.D., professor of microbiology, University of Pennsylvania, Philadelphia; Charles A. Perera, M.D., associate clinical professor of ophthalmology, Columbia University College of Physicians and Surgeons, New York; Lorrin A. Riggs, Ph.D., professor, Department of Psychology, Brown University, Providence; Samuel L. Saltzman, M.D., assistant clinical professor of ophthalmology, New York Medical College, Flower and Fifth Avenue Hospitals, New York; Kenneth C. Swan, M.D., chief, Department of Ophthalmology, University of Oregon Medical School, Portland; and Phillips Thygeson, M.D., professor of ophthalmology, University of California School of Medicine, San Francisco.

#### SOCIETIES

##### CONNECTICUT CHAPTER

In March, the Connecticut Committee of the National Society for the Prevention of Blindness was granted the first charter by the national society and the first annual meeting of the newly organized chapter was held on May 2nd. Officers elected were Mr. Stanley F. Withe, of The Aetna Casualty and Surety Company of Hartford, president; Dr. Ira V. Hiscock of the Department of Health, Yale University, vice-president and consultant; and Dr. Eugene M. Blake, vice-president and medical director.

##### NASSAU MEETING

At the April meeting of the Nassau Ophthalmological Society held at Hempstead, New York, Dr. I. S. Tassman, Philadelphia, presented a paper on "Diabetic retinopathy."

##### OFFICERS OF GEORGIA SOCIETY

At the spring meeting of the Georgia Society of

Ophthalmology and Otolaryngology held recently in Savannah, Georgia, the following officers were elected: President, Dr. Alton V. Hallum, Atlanta; vice-president, Dr. W. L. Barton, Macon; secretary-treasurer, Dr. W. P. Rhyne, Albany.

Guest lecturers at the two-day meeting were: Dr. Francis Heed Adler, Philadelphia; Dr. James H. Allen, New Orleans; Dr. Walter H. Fink, Minneapolis; Dr. Jerome A. Hilger, St. Paul; Dr. J. W. McCall, Cleveland; and Dr. P. E. Ireland, Toronto.

##### MADRID SOCIETY OFFICERS

Officers elected at a recent meeting of the Madrid Ophthalmological Society were: President, Dr. M. Marin-Amat; vice-president, Dr. J. Arjona Trapote; secretary, Dr. J. L. del Rio Cabañas; treasurer, Dr. M. Rios Sasiain; and director, Dr. G. Leoz de la Fuente.

##### KANSAS CITY POSTGRADUATE COURSE

Guest instructors for the postgraduate course in ophthalmology and otolaryngology, sponsored by the Kansas City Society of Ophthalmology and Otolaryngology and held recently at Kansas City, Missouri, were:

Dr. James H. Allen, New Orleans; Dr. Bernard Becker, Saint Louis; Dr. Noah D. Fabricant, Chicago; Dr. Leland G. Humnicutt, Pasadena; Dr. Alexander R. Irvine, Jr., Los Angeles; Dr. Raymond E. Jordan, Pittsburgh; Dr. V. Everett Kinsey, Detroit.

##### CENTRAL ILLINOIS MEETING

At the 24th convention of the Central Illinois Society of Ophthalmology and Otolaryngology, held recently at Springfield, Illinois, the following papers of ophthalmic interest were presented:

"Opportunities for strengthening prevention of blindness efforts," Mrs. Ben Humphries Gray, executive secretary of the Illinois Society for the Prevention of Blindness, Chicago; "Conjunctival and corneal surgery," Dr. Alfred E. Maumenee, Palo Alto, California; "Late divergence complicating convergent squint surgery," Dr. Frederick A. Crowley, Bloomington, Illinois; "Elevated lesions in the posterior fundus," and "Surgery of complicated cataract," Dr. Maumenee.

##### MASSACHUSETTS MEETINGS

The meeting of the Eastern Section of the Association for Research in Ophthalmology which preceded the annual meeting of the Massachusetts Eye and Ear Alumni Association, was held in Boston on April 25. At the alumni meeting which convened on April 26, the following papers were presented before the ophthalmologic section:

"A survey of the more popular types of post-enucleation implants in use today," Dr. William Stone, Jr.; "A rare form of hereditary epithelial dystrophy of the cornea," Dr. L. Byerly Holt; "A heretofore undescribed heredo-congenital corneal dystrophy," Dr. David D. Donaldson; "Some ob-

servations of Duane's syndrome," Dr. Trygve Gundersen and Dr. Bernard Zeavin; "Unilateral proptosis," Dr. Edwin B. Dunphy; "Atrophy of the iris, corneal edema, and glaucoma," Dr. Paul A. Chandler; "Diseases of the optic nerve," Dr. Frank D. Carroll; "Observations on the influence of new drugs on intraocular pressure," Dr. Robert R. Trotter. Dr. William P. Beetham presided at this session.

At the second session, Dr. Paul A. Chandler, presiding, Dr. Mahlon T. Easton spoke on "Complications of bilateral cataract extraction"; Dr. W. Morton Grant, "Outflow measurements in enucleated eyes"; Dr. Charles L. Schepens, "Evaluation of scleral buckling procedures"; Dr. David G. Cogan, "Paralimbal keratitis and scleritis occurring as part of a fatal systemic disease"; Dr. Sunny J. Bullerton, "The quantitative Arthus' phenomenon in the rabbit"; Dr. Robert J. Herm and Dr. Parker Heath, "A study of retinoblastoma"; Dr. Marvin Posner, "A method of excising a lesion involving the lower punctum"; Dr. M. C. Twitchell, Jr., "The mechanical eye and the electrical eye."

Dr. Frank W. Dimmitt presided at the third session when the following papers were read: "Presentation of cases," Dr. Richard Chapman; "Pathology conference," Dr. Taylor R. Smith; "Preplaced catgut suture in cataract extraction," Dr. Richard H. Dennis; "The so-called blindspot mechanism," Dr. Frederick H. Verhoeff; "Highlights of glaucoma," Dr. Paul A. Chandler.

#### AMERICAN OPHTHALMOLOGICAL SOCIETY

The following papers will be presented at the 91st annual meeting of the American Ophthalmological Society to be held at the Greenbrier, White Sulphur Springs, West Virginia, on June 2, 3, and 4, 1955.

"The progress of ophthalmology throughout the world: A challenge to leading ophthalmologists," Dr. Moacyr E. Alvaro, São Paulo, Brazil; "The importance of ophthalmoscopic photographs in forensic medicine," Dr. Arthur J. Bedell, Albany, New York; "Essential atrophy of the iris, endothelial dystrophy, corneal edema, and glaucoma," Dr. Paul A. Chandler, Boston; "Some automatic and semi-automatic trephines, including an electric trephine with automatically retracting blade," Dr. Frederick H. Verhoeff, Boston; "Total and permanent blindness following administration of hexamethonium chloride," Dr. Gordon M. Bruce, New York; "Absence of the internal rectus and its successful treatment by vertical tendon transplants," Dr. Howard F. Hill, Waterville, Maine; "Results of combined operation for cataract and glaucoma," Dr. Wendell L. Hughes, Hempstead, New York; "Peri-orbital fibrous dysplasia," Dr. Ralph O. Rychener and Dr. Francis Murphey, Memphis, Tennessee; "Use of carbonic anhydrase inhibitor acetazolamide (Diamox) for endothelial corneal dystrophy and diseased corneal grafts," Dr. Frederick W. Stocker, Durham, North Carolina; "A safe section for cataract extraction," Dr. Walter S. Atkinson, Watertown,

New York; "Methods of gonioscopy," Dr. Robert N. Shaffer, and Dr. Robert Tour, San Francisco; "Glial tumors of the retina in relation to tuberculous sclerosis," Dr. John M. McLean, New York; "Myopia caused by prematurity," Dr. Henry L. Birge, Hartford, Connecticut; "Some causes of enucleation after cataract extraction," Dr. Brittain Ford Payne, Dr. John T. Simonton, and Dr. Dahar Cury, New York; "Progressive nuclear ophthalmoplegia," Dr. William John Holmes, Honolulu; "Tumors of the lacrimal gland: Their prognosis," Dr. T. E. Sanders and Dr. L. V. Ackerman, Saint Louis; "Intraocular pressure evaluations with paredrine hydrobromide," Dr. F. L. Philip Koch, Bronxville, New York, Louis H. Darley, New York, and Dr. Paul Levatin, Oakland, California; "Tonography and the management of glaucoma," Dr. Harold G. Scheie, Dr. Robert W. Spencer, and Dr. Ernest D. Helmick, Philadelphia; "Aqueous pathways in some cases of glaucoma," Dr. Georgiana Dvorak-Theobald and Dr. Harold Quentin Kirk, Oak Park, Illinois; "Paralimbal keratitis and scleritis associated with a fatal systemic disease," Dr. David G. Cogan, Boston.

#### PERSONAL

Dr. Arthur J. Bedell of Albany, New York, has received the University of Buffalo Howe Medal in recognition of "contributions made in research and clinical ophthalmology." The medal was presented by Dr. Stockton Kimball, dean of the University of Buffalo Medical School, at a dinner on April 14. The Lucien Howe Memorial meeting is sponsored by the Buffalo Ophthalmologic Club.

The fund for the medal was established over 30 years ago by Dr. Lucien Howe, professor emeritus of ophthalmology and for over a quarter century a teacher of ophthalmology at the University of Buffalo.

Dr. Bedell has extensive background and experience in the field of ophthalmology. He was graduated from Albany Medical College in 1901 and continued his studies abroad in European clinics. He joined the faculty of Albany Medical College in 1907 and headed the eye department there from 1913-27. In 1941 he was named professor emeritus of ophthalmology.

Dr. Bedell received the American Medical Association Silver Medal for a scientific exhibit in 1928; the Herman Knapp Gold Medal for outstanding work in ophthalmology from the Ophthalmology Section of the AMA in 1929, the Medal for Distinguished Service to Ophthalmology of the Section on Ophthalmology, A.M.A., 1952; and the Lucien Howe prize for research in ophthalmology from the New York State Medical Society in 1922, 1924, 1927, 1936, and 1938. He was a lecturer at Oxford University in England during 1936.

Dr. Bedell is a member of many ophthalmology societies both here and abroad. Also, he is the author of over 100 monographs and articles and is a former associate editor of the *Annals of Ophthalmology*.

---

## *The Purpose of the Guild*

---

- The aim of the Guild of Prescription Opticians of America is to advance the science of ophthalmic optics through the development of a country-wide ethical optical dispensing service that comprehensively meets the needs of the Eye Physicians and their patients; and to educate the public to the fact that the Eye Physician-Guild Optician type of eye service truly renders the most desirable form of eye care.

*This statement of the Guild's purpose is reprinted from the cover of the REFERENCE LIST OF GUILD OPTICIANS, a geographical index of all our members. If you would like a copy, just drop a two-penny post card to*

**The Guild of Prescription  
Opticians of America, Inc.**

110 E. 23rd Street New York (10) N.Y.

## ATTRACTS NEW ALLOY STEELS THAT SMALL MAGNETS DO NOT MOVE

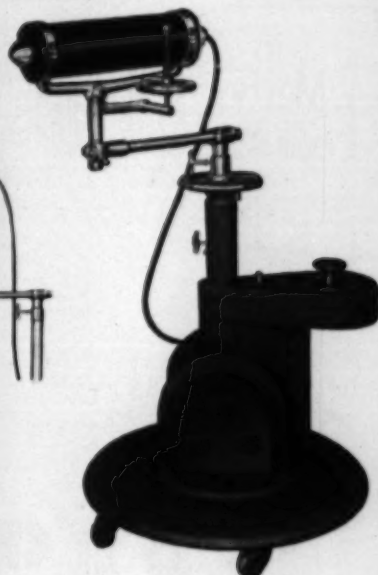
*The New Improved Mueller*

## GIANT EYE MAGNET

Now equipped with a spark-free, noiseless selenium rectifier and explosion-proof footswitch control, the Mueller Giant Magnet is better—safer—surer than ever—essential equipment for the modern hospital, clinic, industrial first aid room. Greater power than any comparable magnet provides a much increased range of usefulness, particularly in removal of bits of the newer alloys which are not affected by smaller magnets. Perfectly counterbalanced, the magnet is quickly and silently adjustable in height, direction and tilt—as easy to operate as it is free from maintenance costs. On noiseless casters, complete with interchangeable blunt and probe pointed silvered tips. Early delivery. Write for details.



*Adjustable  
in Height,  
Direction  
and Tilt*



*V. Mueller & Co.*

330 SOUTH HONORE STREET  
CHICAGO 12, ILLINOIS

## GREEN'S ELECTRIC TREPHINE

IMPROVED MODEL BY DAVID KADESKY, M.D.



The instrument simplifies the operation of trephining for Glaucoma or Corneal Transplantation. Blades are provided with a shoulder that prevents penetration beyond 1.1 mm., and are available in 1½ mm., 4.5, 4.6, 5.5, 5.6, 6.5, 6.6, mm. diameters.

Trephine, case, and two 1½ mm. blades .....\$95.00

PARSONS OPTICAL LABORATORIES, INC.

518 Powell Street

San Francisco 2, Calif.





Sterile, buffered ophthalmic suspensions of Cortisone Acetate and Hydrocortisone Acetate for topical use. In Methyl Cellulose for more uniform suspension, more prolonged contact (5 to 6 times longer), and better dispersion when applied to the eye.

#### ADVANTAGES OF DROP-TAINER PRODUCTS

- Sterile      • Stable      • Preserved against contamination
- Convenient to carry and use: better drop control
- Economical: non-spillable and non-breakable      • Uniform

Available from pharmacies and wholesale drug suppliers throughout the U.S.A. and Canada (Canadian Distributors, Imperial Optical Company, Toronto, Canada). Write for catalog descriptive of miotics, mydriatics, anesthetics, etc., supplied in Drop-Tainer.

## Alcon

LABORATORIES, INCORPORATED  
FORT WORTH, TEXAS

# *E. B. Meyrowitz*

**SURGICAL INSTRUMENTS CO., INC.**  
**520 FIFTH AVENUE, NEW YORK 36, N.Y.**

**LONDON**

**ESTABLISHED 1875**

**PARIS**

**PLASTIC REGAN ASTIGMATIC CHARTS**

(Copyright 1951)

*Designed by Dr. J. J. Regan of Boston*

The Regan Astigmatic Test Charts are for the purpose of determining the axis of astigmatism and its amount, by the subjective method. The charts are to be used in conjunction with trial case lenses or refractor. These charts will be found especially useful in determining small amounts of astigmatism and accurately determining the axis.

Chart No. 1 consists of thirty-six radiating lines ten degrees apart, and is to be used during the first part of the examination for determining the approximate axis of astigmatism—later the exact axis of astigmatism.

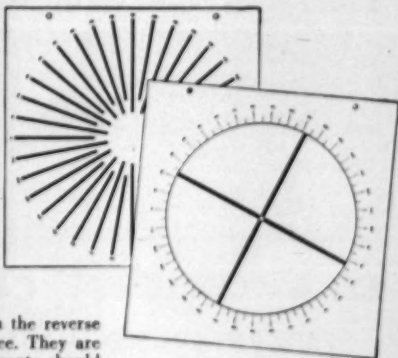
Chart No. 2 has a rotating dial showing two black lines at right angles to each other. The front of this chart can be rotated so that the lines will occupy any desired position. Chart No. 2 is used in determining the amount of astigmatism and final checking of the axis.

Brief instructions for obtaining best results are printed on the reverse side of both dials. These charts are permanent and warp-free. They are best cleaned with mild soap and water. Art gum and detergents should not be used. Size of each chart 15" x 15". Shipping weight 2½ lbs.

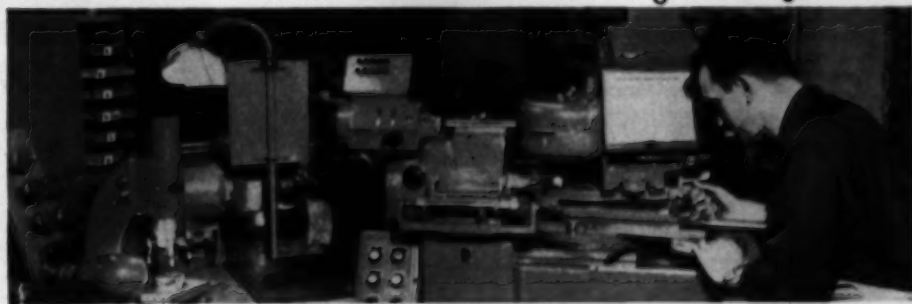
**Price of the set of two Plastic Charts—\$15.00**

Lancaster-Regan Charts, same size as above, cardboard, set of 2 ..... \$ 4.50

Lancaster Charts, Metal (in Shadow Box Form), No. 1 Chart 24½" sq., No. 2 Chart 18½" sq., set of 2 ..... \$55.00



## *Here, in Benson's Laboratories, you'll find...*



### **Men and Machines**

In manufacturing optical products which *must* be precise, the skill of master craftsmen is essential. Add to that skill the most modern production equipment and you have a combination unsurpassed.

Forty-two years of continuous growth have produced BENSON branches in 27 cities of the Upper Midwest . . . laboratories where prescriptions are *accurately* transformed into fashionable glasses. And the "BENSON" name has come to stand for the highest quality and precision in optical production.

*May we serve you?*

Since 1913

**Benson**

Executive Offices • Minneapolis, Minn.

COMPLETE LABORATORIES CONVENIENTLY LOCATED IN UPPER MIDWEST CITIES

ST. LOUIS, MO.

**Erker Bros. Optical Co.**

908 Olive Street  
 518 N. Grand Boulevard  
 and 33 N. Central Ave., Clayton, Mo.  
 Prescription Opticians Since 1879

**Dow Optical Co.**  
PRESCRIPTION SPECIALISTS

Suite 1015 30 N. Michigan Avenue  
 Chicago, Illinois  
 Phone RAndolph 6-2243-44

DEALERS IN OPHTHALMOLOGICAL  
 EQUIPMENT

The Sixth Annual Meeting of the New Orleans Academy of Ophthalmology will be held in New Orleans, Roosevelt Hotel, January 3-6, featuring "Diseases and Surgery of the Lens". The registration fee of \$75.00 includes membership in the Academy for the year 1956. Hotel reservations should be made early by writing to the Roosevelt or 211 S. Saratoga St., New Orleans, La.

CHICAGO, ILL.

**ALMER COE & COMPANY**

Prescription Opticians

Established 1886

10 N. Michigan Ave.  
 1646 Orrington Ave., Evanston, Ill.

PORTLAND, ORE.

Hal. H. Moor, 315 Mayer Bldg.



Guild Optician

Oculists' prescriptions exclusively

CINCINNATI, OHIO

L. M. Prince Co.

Established 1872

Prescription Opticians

Sole makers of Coefflex

Corrected Curve Lenses

BRoadway 6336

**PAUL G. DAVIES**

DISPENSING OPTICIANS

Prescriptions of Eye Physicians exclusively

906 S. W. TAYLOR ST.

PORTLAND 5, OREGON

## NEW PLASTIC CLIP-ON PRISMS

These new prisms may be worn for trial purposes while the eyes are performing the work for which the correction is prescribed, proving that the prescription will be most helpful and comfortably worn.

Prisms are round making it possible to rotate to any axis and are made in two sizes 40 mm. and 44 mm.

Set contains 1 pair each 1-2-3 4-5-6 diopters with four frames and small screwdriver.



Price \$30.00

*Available at all Optical and Surgical Suppliers.*

*Manufactured by*

4920 N. Lawrence St.

R. O. GULDEN

Philadelphia 20, Pa.

*Spectel*  
TELESCOPIC  
SPECTACLES



**2.2x**  
(with Coated Lenses)

**WHAT THEY ARE.** A general discussion of the design, construction and uses of the improved Spectels. An outline of their development. Comparisons of the two magnifications and descriptions of the various trial sets. Bulletin 302.

**HOW THEY ARE PRESCRIBED.** Twelve pages of factual information on the application of telescopic spectacles. Case histories. Bulletin 304.

**TRIAL PROCEDURE.** A concise, step-by-step outline of the trial procedure which has been found effective. Bulletin 303.

**TRIAL SETS.** Complete descriptions and illustrations of the four different trial sets available. Form 85.

**PRICES** of Spectel telescopic spectacles, frames, trial sets and accessories are given in Form 7146-A.

This literature is available from your supply house or from



**KOLLMORGEN**

Plant: Northampton, Massachusetts

New York Office: 30 CHURCH ST., NEW YORK 7, N. Y.

*Optical* CORPORATION

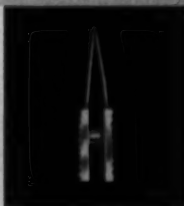
Distributed in Canada by  
Imperial Optical Company

**LAWTON****Corneoscleral Suture Forceps** by John J. Sauer, M. D.

This new suture forceps has been designed to afford firm fixation of the cornea or sclera with a minimum amount of tissue trauma.

The over-all length of the instrument is 70 mm. The shaft is 13 mm long and 1.0 mm wide. The forceps has 1x2 angular teeth, which are 0.6 mm long and very strong. A stop prevents excessive overlapping of the teeth, thereby limiting the bite into the tissue. The forceps will not hold the conjunctiva, the latter sliding free between the teeth. Stainless Steel \$7.00 each.

Available Only Through Authorized Surgical Supply Dealers.



THE *Lawton* COMPANY • 425 FOURTH AVE., NEW YORK 16, N.Y.



## FOR THE DRY EYE METHISOL

METHYLCELLULOSE 4000 cps 1/2%

APPROXIMATES THE VISCOSITY OF TEARS  
INDEX OF REFRACTION OF CORNEA.

STERILE ISOTONIC SOLUTION in  
DROPPER-SEALED BOTTLES 15 cc.

### INDICATIONS

SJÖGREN'S SYNDROME  
KERATOCONJUNCTIVITIS SICCA  
BELL'S PALSEY

OTHER OCULAR CONDITIONS  
WHERE LACK OF TEARS IS A SYMPTOM  
EXCESSIVE EXPOSURE TO SUN AND WIND  
AND ATMOSPHERIC IRRITANTS

ALLEVIATES DISCOMFORT  
PROTECTS THE CORNEA  
LUBRICATES THE GLOBE

**OPHTHALMOS, INC.**

**Union City, N. J.**

IN PUERTO RICO AND VIRGIN ISLANDS AVAILABLE THROUGH ALL WHOLESALERS

IN CANADA DISTRIBUTED BY **PROFESSIONAL SALES CORP.**, Montreal 29, Quebec

METHISOL IS A TRADEMARK OF OPHTHALMOS, INC.





## **PRESCRIPTION SERVICE FOR ALLERGIC DISEASES**

### **Allergenic Extracts, Diagnostic and Therapeutic**

Devoted exclusively to the manufacture of pollen, fungus, epidermal, food, dust, and miscellaneous allergenic extracts for the diagnosis and treatment of allergic conditions.

A pollen check list for your state and other literature sent on request.

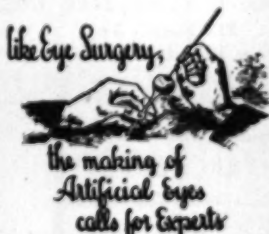
U.S. Government License No. 103 since 1929

### **ALLERGY LABORATORIES, INC.**

Pasteur Medical Building

Oklahoma City 1, Oklahoma

1111 N. Lee Avenue



### **GREINER & MUELLER**

Expert makers  
of artificial human eyes

#### **GLASS & PLASTIC**

55 E. Washington St. . . . Chicago 2, Ill.

Phone FR 2-4449

Branches at Kansas City, Mo., Detroit, Mich.

Our experts visit Milwaukee, Madison, Minneapolis, and St. Louis regularly. Serving the Middle West since 1934.

Eye making has been a family tradition  
with us since 1835.

## **"LACRILENS" is a safe lens**

The test of time proves that the "LACRILENS"® contact lens can be worn for long periods of time in aphakia and in all sports, including swimming.

Write for Brochure

Manufacturers of  
all types of  
Contact Lenses

*Obrig Laboratories Inc.*

49 East 51st Street, New York 22, N. Y.



Branches in PHILADELPHIA • MONTREAL • JOHANNESBURG

**POSTGRADUATE COURSE  
and  
SUMMER CONVENTION OF  
THE COLORADO  
OPHTHALMOLOGICAL  
SOCIETY  
and the  
UNIVERSITY OF COLORADO  
MEDICAL CENTER  
Denver, Colorado**

**July 25, 26, 27, 28, 1955**

The program will consist of lectures, seminars and demonstrations of interest to both the specialist and the practitioner caring for Eye Diseases.

Registration will be open to all members of the Society and qualified physicians on a limited membership basis. Tuition \$40.00.

Plan now to attend and combine an intensive review of advances in this specialty with your summer vacation.

Complete program and details will be mailed upon request addressed to:

Director of Postgraduate Medical Education  
University of Colorado School of Medicine  
4200 East Ninth Avenue  
Denver 20, Colorado

**"OPHTHALMIC  
LITERATURE"**

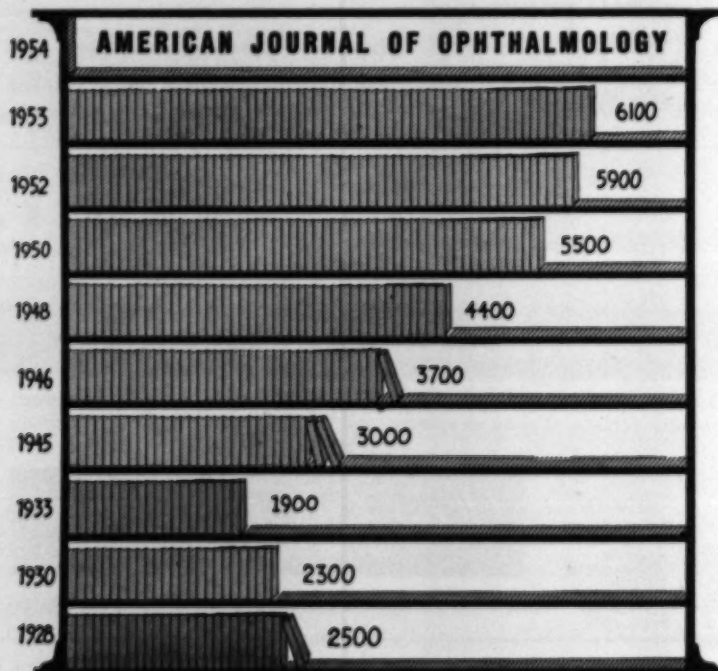
**AN ABSTRACT JOURNAL IN ENGLISH OF THE WORLD'S CURRENT LITERATURE ON OPHTHALMIC SUBJECTS**

Indispensable to the busy practitioner for quick reference and timely useful information.

"Ophthalmic Literature" and Index (8 numbers) Yearly subscription—Four Guineas (\$13.50 U.S.A.). Published by British Medical Association.

U. S. A. Agent

**GRUNE & STRATTON, INC.**  
381 Fourth Ave.  
New York 16, New York



# THE BRITISH JOURNAL OF OPHTHALMOLOGY

*Published monthly by*

The British Medical Association

Annual Subscription \$13.50



## OPHTHALMIC LITERATURE

A comprehensive quarterly abstract of  
ophthalmology and cognate literature.

Annual Subscription \$13.50



Subscriptions to:

GRUNE AND STRATTON, INC.

381 Fourth Avenue

New York 16

New York, U.S.A.

# Ophthalmologica

International Journal of Ophthalmology  
Journal international d'Ophthalmologie  
Intern. Zeitschrift für Augenheilkunde

Organ der Schweizerischen Ophthalmologischen Gesellschaft - Organe de la Société Suisse d'Ophthalmologie. Organ van het Nederl. Oogheelkundig Gezelschap - Organ of the Nederl. Ophthalm. Society

## Editores:

### Aegyptus:

M. Sobhy Pasha  
R. P. Wilson\*

### Africa:

#### Meridionalis:

A. Jökl  
R. C. J. Meyer\*  
J. S. du Toit

### America:

F. H. Adler  
H. Barkan  
E. V. L. Brown\*  
J. S. Friedenwald  
P. Heath  
Bertha Klien  
A. C. Krause  
B. Samuels  
Ph. Thygeson  
F. H. Verboeff  
A. C. Woods  
A. M. Yudin

### Argentina:

F. Belgeri\*  
B. Courtis  
M. Dusseldorp  
R. Gil  
G. v. Grolman

### Australia:

J. R. Anderson\*  
J. A. Flynn

J. B. Hamilton  
M. Schneider

### Belgica:

M. Appelmans\*  
L. Coppes  
L. Hambresin  
A. van Lint  
A. van der Straeten  
L. Weekers

### Brazilia:

M. Alvaro\*  
C. de Andrade  
I. Correa-Meyer  
P. Pimentel  
L. Silva

### Britannia:

A. J. Ballantyne\*  
St. Duke-Elder  
C. B. Goulden  
Ida Mann  
W. C. Souter

### Chile:

C. E. Luca\*

### Dania:

H. Ehlers  
H. Rønne\*

### Finlandia:

Hilja Teräskell  
M. Vannas\*

### Gallia:

E. Anbaret  
P. Bailliet\*  
R. Bidault  
J. Bollack  
P. Bonnet  
C. Bourdier  
Jean-Gallois  
G. Jayle  
P. Jeandelise  
H. Lagrange  
P. Lemoine  
J. Mawas  
J. Nordmann  
R. Onfray  
L. Pautique  
E. Redslob  
Jean-Sédan\*  
G. P. Sourdille  
R. de Saint Martin  
Mme S. Schiff  
Ch. Thomas  
G. Valois  
E. Velter  
G. Weill

### Graecia:

B. Adamantiades  
J. Bistis\*  
J. Charamis  
G. F. Cosmetatos  
N. Dascalopoulos  
C. A. Gabriélides  
Th. Tjanidis  
A. Trantas  
N. G. Trantas

### Helvetia:

M. Amstler  
A. Franceschetti  
H. Goldmann  
E. B. Streiff

### Hispania:

H. Arruga\*

### Hollandia:

H. M. Dekking  
J. van der Hoeve  
A. W. Mulock  
Houwer  
G. F. Rochat

### Hungaria:

G. Ditrói  
St. v. Gróss  
G. Horay  
A. Kettesy  
T. Nónay

### India Orient.

### Neerlandica:

J. G. van Manen\*

### Italia:

B. Alajmo  
G. Lo Cascio  
Q. di Marzio\*

### Luxemburgia:

A. Faber

Ch. Israel  
A. Ketter  
G. Schtingen

### Palaestina:

A. Feigenbaum\*

### Polonia:

W. Kapuscinski

### Portugal:

A. L. de Andrade  
S. Senna

### Romania:

N. Blatt

### Tszechoslovacia:

R. Kadlík  
J. Kublík

### Tunesia:

R. Nataf\*

### Turcia:

N. I. Gösoň

### Uruguay:

V. Barrière\*

\* Editor principalis

Redactores: A. BRÜCKNER-Basel, H. WEVE-Utrecht

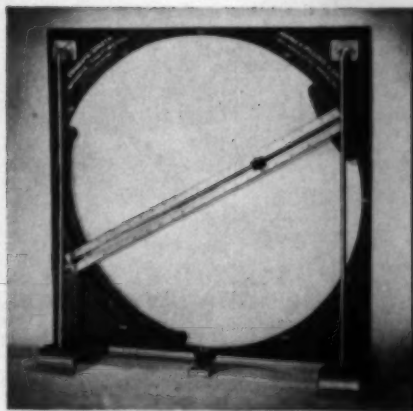
It is the task of "Ophthalmologica" to advance our knowledge in Ophthalmology by stimulating international co-operation. We publish:

1. Papers in English, German and French.
2. Reviews. One or more subjects of Ophthalmology will be reviewed every month, so that the reader will obtain a comprehensive survey of all the publications which have appeared during the past year.
3. Notes on practical questions. These columns are to be devoted to short interesting observations on cases occurring in everyday practice. They will appear in concise form, perhaps accompanied by an illustration.
4. Reports about the activities of ophthalmological societies.
5. Book Reviews. News.

2 volumes of 6 parts each are published yearly. Subscription price U.S. \$10 per volume plus \$.60 postage

S. KARGER PUBLISHERS, BASEL, SWITZERLAND

For U.S.A.: Albert J. Phibbs  
345 Fifth Avenue, New York 17, New York



*Conover-Spaeth\**

## MAGNETIC CAMPIMETER

\*EDMUND B. SPAETH, M.D.

PHILADELPHIA, PA.

This new precision instrument gives accurate determinations and correct configuration of the visual field with great savings of time and effort.

The Conover-Spaeth Campimeter is 24" square. It is placed on a table with the patient seated in front, his eye positioned 10½" from the central fixation point. The operator, standing behind the screen, facing the patient and looking directly into the patient's eye, is able to detect the slightest wavering. The test object is introduced to the visual field from a "Concealment Circle" and is controlled by a magnet from the back of the campimeter. The patient is not able to anticipate or even guess on

which radius or from which side, right or left, the test object will appear.

This assures accuracy and eliminates time-consuming rechecking.

The back of the campimeter is clearly marked in degrees of the circle and angles of vision to conform to the standard Berens chart. Each radius tested is immediately entered on the chart . . . No markers to be placed or removed.

The time saved in each examination creates opportunities for more "fields" or other office work.

✓ **ABSOLUTE ACCURACY**

✓ **FAR FASTER**

Write for detailed information.

### DISPENSING SERVICE

Main Office:  
109 N. Wabash Ave., at Wash.  
Chicago, Illinois



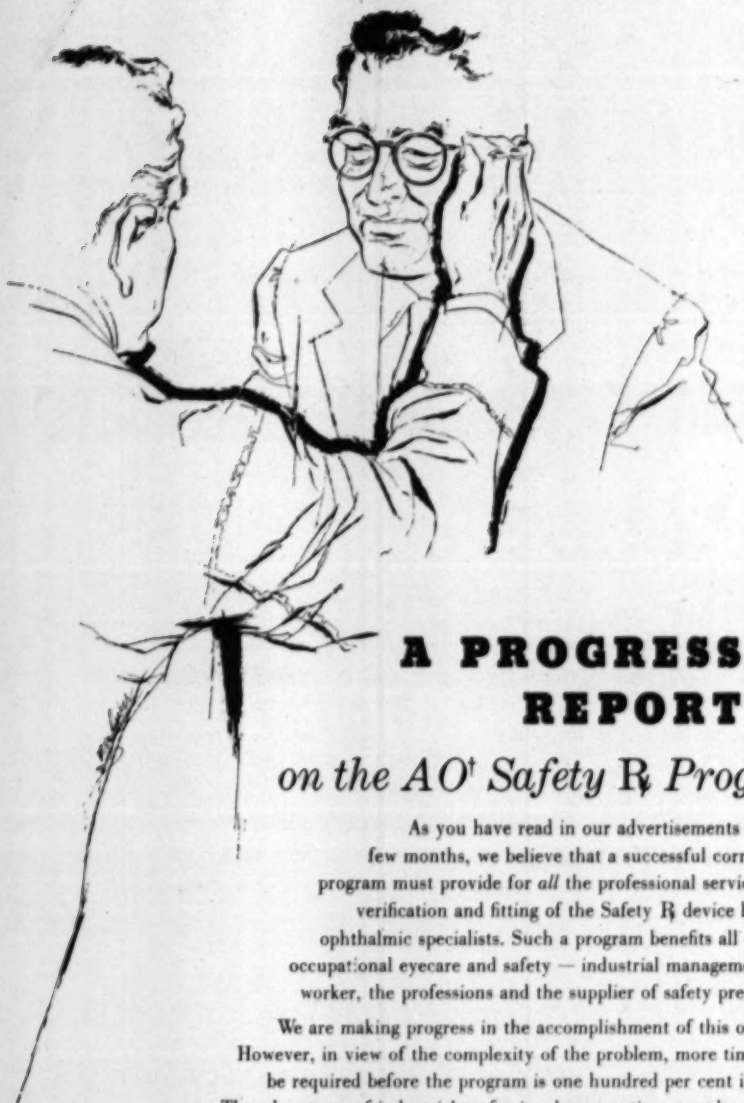
INC.

(formerly Belgard, Inc.)

OPHTHALMIC  
OPTICIANS  
Wholesale & Service

Branch Offices:  
1920 W. Harrison St. at Ogden  
1139 Central Ave., Wilmette, Ill.





## **A PROGRESS REPORT**

### *on the AO<sup>†</sup> Safety R<sub>2</sub> Program*

As you have read in our advertisements over the past few months, we believe that a successful corrective-protective program must provide for *all* the professional services. This includes verification and fitting of the Safety R<sub>2</sub> device by qualified ophthalmic specialists. Such a program benefits all concerned with occupational eyecare and safety — industrial management, the individual worker, the professions and the supplier of safety prescription devices.

We are making progress in the accomplishment of this objective. However, in view of the complexity of the problem, more time will be required before the program is one hundred per cent in operation. The advantages of industrial-professional cooperation must be explained to industry almost on a company by company basis, nationally.

Industry, in turn, must make important decisions as to their methods of operation with the professions and these arrangements will necessarily vary.

For our part, we are using every effort to expedite the program as rapidly as possible.

# American Optical

